STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 139335

TO: Michael Meller **Location: REM-3C08/3C18** **Art Unit: 1654** **Monday, December 06, 2004** **Case Serial Number: 09/889414**	**From: Edward Hart** **Location: Biotech-Chem Library** **REM-1A55** **Phone: 571-272-2512** **edward.hart@uspto.gov**

Search Notes

Examiner Meller,

Here are the results of the search you requested.

Please feel free to contact me if you have any questions.

Edward Hart

139335

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Mike Meller Examiner #: 69404 Date: 12/2/04
Art Unit: 1654 Phone Number ~~571-272-0677~~ Serial Number: 09/688,414
Mail Box and Bldg/Room Location: Rem 3C03. Results Format Preferred (circle): PAPER, DISK, E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Drug Combinations Comprising (E)-7-(4-(4-Fluo...

Inventors (please provide full names): John S. Pears, Ali Raza, Hyland Hutchinson, Dennis Schneck, Takahiko Baba, Akira Iguchi, Yoshitaka Yamaguchi

Earliest Priority Filing Date: 6/2/1999

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

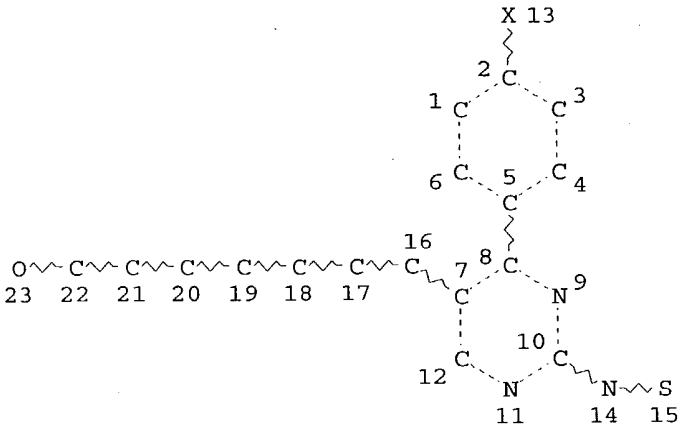
Please Search the "First Drug" in claim 1 (the (E)-7-(4-(4-...) with the compounds in claim 5 (benzafibrate...etc.) Search where both are together. Don't have to search separately, just that they are together.

C. Chan

Rush

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher _____	NA Sequence (#) _____	STN _____
Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up _____	Bibliographic _____	Dr.Link _____
Date Completed: 12/6/04	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time _____	Patent Family _____	WWW/Internet _____
Online Time _____	Other _____	Other (specify) _____

PTO-1590 (8-01)



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

L13	36	SEA FILE=REGISTRY SUB=L11 SSS FUL L12
L14	1	SEA FILE=REGISTRY ABB=ON PLU=ON C21H26FN3O6S/MF AND L13
L15	1	SEA FILE=REGISTRY ABB=ON PLU=ON BEZAFIBRATE/BI
L16	35	SEA FILE=REGISTRY ABB=ON PLU=ON CLOFIBRATE/BI
L17	5	SEA FILE=REGISTRY ABB=ON PLU=ON CIPROFIBRATE/BI
L18	1	SEA FILE=REGISTRY ABB=ON PLU=ON FENOFIBRATE/BI
L19	19	SEA FILE=REGISTRY ABB=ON PLU=ON NIACIN/BI
L20	291	SEA FILE=HCAPLUS ABB=ON PLU=ON L13
L21	30194	SEA FILE=HCAPLUS ABB=ON PLU=ON (L14 OR L15 OR L16 OR L17 OR L18 OR L19) OR BEZAFIBRATE OR CLOFIBRATE OR CIPROFIBRATE OR FENOFIBRATE OR NIACIN
L22	66	SEA FILE=HCAPLUS ABB=ON PLU=ON L20 AND L21
L23	1	SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND PD<=FEBRUARY 1,2000

=> d ibib abs hitstr l23 tot

L23 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:633275 HCAPLUS
DOCUMENT NUMBER: 139:169333
TITLE: Novel anticholesterol compositions and method for using same
INVENTOR(S): Dudley, Robert; Liao, Shutsung; Song, Ching
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S. Ser. No. 137,695.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003153541	A1	20030814	US 2002-174934	20020619
WO 9922728	A1	19990514	WO 1998-US23041	19981030 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6576660	B1	20030610	US 2000-530443		20000428
US 6645955	B1	20031111	US 2000-560236		20000428
ZA 2001009793	A	20030228	ZA 2001-9793		20011128
CA 2438221	AA	20020815	CA 2002-2438221		20020207
EP 1385868	A2	20040204	EP 2002-704407		20020207

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2002107233	A1	20020808	US 2002-72128		20020208
US 2002193357	A1	20021219	US 2002-137695		20020502
WO 2004001002	A2	20031231	WO 2003-US19515		20030619
WO 2004001002	A3	20040506			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004152681	A1	20040805	US 2003-705398		20031110

PRIORITY APPLN. INFO.:

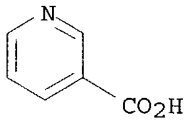
US 1997-63770P	P	19971031
WO 1998-US23041	W	19981030
US 1999-131728P	P	19990430
US 2000-530443	A2	20000428
US 2000-560236	A2	20000428
US 2001-267493P	P	20010208
US 2001-288643P	P	20010503
US 2001-348020P	P	20011108
US 2002-72128	A2	20020208
US 2002-137695	A2	20020502
US 2000-191864P	P	20000324
WO 2002-US3826	W	20020207
US 2002-174934	A	20020619

OTHER SOURCE(S): MARPAT 139:169333

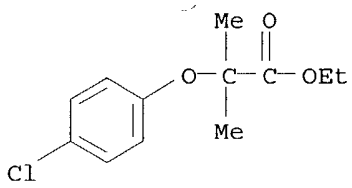
AB Disclosed are compns., methods, combinations, and kits for treating a disorder related to elevated serum cholesterol concentration, for example, atherosclerosis, elevated LDL plasma levels, low HDL plasma levels, hypertriglyceridemia, hyperlipidemia, hypertension, hypercholesterolemia, cholesterol gallstones, lipid storage diseases, obesity, and diabetes. The compns., methods, combinations, and kits of the present invention are pharmaceutical compns. comprising at least two of an LXR receptor modulator, a therapeutically effective amount of a catechin, and/or a therapeutically effective amount of a lipid regulating agent, such as a HMG-CoA reductase inhibitor, a fibric acid derivative, **niacin**, a bile-acid sequestrant, an absorption inhibitor, probucol, raloxifene and its derivs., an azetidinone compound, and an unsatd. omega-3 fatty acid.

IT **59-67-6**, **Niacin**, biological studies **637-07-0**, **Clofibrate 41859-67-0**, **Bezafibrate 49562-28-9**, **Fenofibrate 287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticholesterol compns. containing LXR modulators and lipid regulating agents)

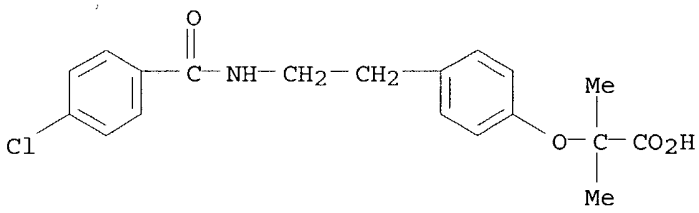
RN 59-67-6 HCAPLUS
CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)



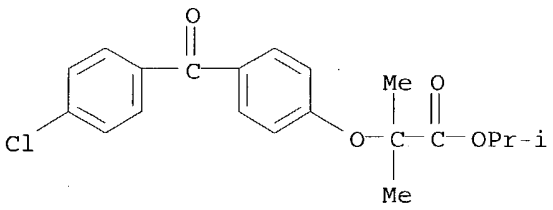
RN 637-07-0 HCAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 41859-67-0 HCAPLUS
CN Propanoic acid, 2-[4-[2-[(4-chlorobenzoyl)amino]ethyl]phenoxy]-2-methyl- (9CI) (CA INDEX NAME)



RN 49562-28-9 HCAPLUS
CN Propanoic acid, 2-[4-(4-chlorobenzoyl)phenoxy]-2-methyl-, 1-methylethyl ester (9CI) (CA INDEX NAME)



RN 287714-41-4 HCAPLUS
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA INDEX NAME)

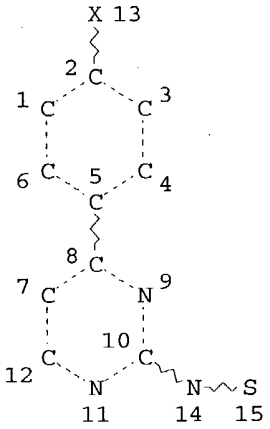
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 15:09:55 ON 06 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 6 Dec 2004 VOL 141 ISS 24
FILE LAST UPDATED: 5 Dec 2004 (20041205/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

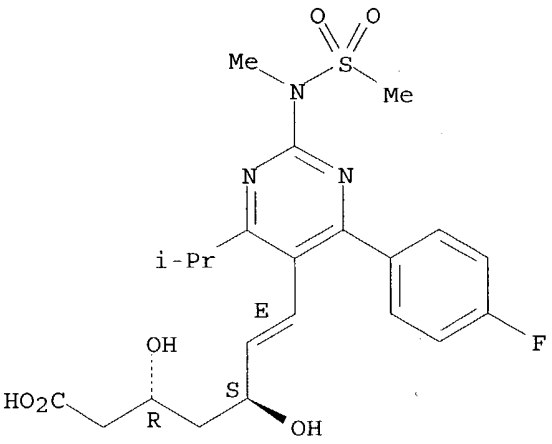
=> d stat que
L9 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L11 94 SEA FILE=REGISTRY SSS FUL L9
L12 STR



=> d ibib abs hitrn l24 tot

L24 ANSWER 1 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:965255 HCAPLUS
TITLE: Preparation of 5,7-diaminopyrazolo[4,3-d]pyrimidines as selective PDE-5 inhibitors useful in the treatment of hypertension
INVENTOR(S): Bell, Andrew Simon; Brown, David Graham; Fox, David Nathan Abraham; Marsh, Ian Roger; Morrell, Andrew Ian; Palmer, Michael John; Winslow, Carol Ann
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 279 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096810	A1	20041111	WO 2004-IB1433	20040422

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-9780 A 20030429
GB 2003-27748 A 20031128

AB Title compds. I.
IT INDEXING IN PROGRESS
IT **637-07-0**, **Clofibrate** **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of 5,7-diaminopyrazolo[4,3-d]pyrimidines as selective PDE-5 inhibitors useful in treatment of hypertension)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:817865 HCAPLUS
DOCUMENT NUMBER: 141:314351
TITLE: Preparation of 1,2,4-substituted 1,2,3,4-tetrahydro- and 1,2 dihydro-quinoline and 1,2,3,4-tetrahydro-quinoxaline derivatives as cetp inhibitors for the treatment of atherosclerosis and obesity
INVENTOR(S): Chang, George; Didiuk, Mary Theresa; Finneman, Jari Ilmari; Garigipati, Ravi Shanker; Kelley, Ryan Michael; Perry, David Austen; Ruggeri, Roger Benjamin; Bechle, Bruce Michael
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 335 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085401	A1	20041007	WO 2004-IB836	20040315
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004204450	A1	20041014	US 2004-807838	20040323
PRIORITY APPLN. INFO.:			US 2003-458274P	P 20030328
			US 2004-536217P	P 20040114

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = C; J = N or C, wherein when J = C, then the bond between J and X is a single or double bond, if J = N, then the bond between J and X is a single bond; R1 = Y, W-Z or W-Y; Y = (un)substituted, (un)saturated 3-8 membered ring (or bicyclic ring) optionally having 1-4 heteroatoms, or (un)substituted, (un)saturated 1-10 membered straight or branched carbon chain optionally substituted with 1-2 heteroatoms; W = carbonyl, thiocarbonyl, sulfinyl, or sulfonyl; Z = OY, SY, NHY or NY2; R2 = (un)substituted, (un)saturated 1-6 membered alkyl or heteroalkyl chain; R3 = (un)substituted, (un)saturated alkyl or heteroalkyl chain; R4, R5, R6, and R7 independently = H, bond, nitro, etc.; or adjacent combinations of R4, R5, R6, and R7 may optionally be taken together to form (un)substituted, (un)saturated carbocycle or heterocyclic ring], and pharmaceutical compns. containing such compds. are prepared and disclosed as cholesteryl ester transfer protein (cetp) inhibitors. Thus, e.g., II was prepared by reaction of 3,5-bistrifluoromethylbenzoyl chloride with 4-diazo-6,7-dimethoxy-2-methyl-3,4-dihydro-2H-quinoline-1-carboxylic acid Et ester (preparation given) in

di-Et ether. Methods for bioassaying compds. I are described (no data). The use of I to elevate certain plasma lipid levels, including high d. lipoprotein-cholesterol and to lower certain other plasma lipid levels, such as LDL-cholesterol and triglycerides and accordingly to treat diseases which are exacerbated by low levels of HDL cholesterol and/or high levels of LDL-cholesterol and triglycerides, such as atherosclerosis and cardiovascular diseases in some mammals, including humans is further disclosed.

IT **59-67-6**, **Niacin**, biological studies **287714-41-4**
, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of quinoline and quinoxaline derivs. as cholesteryl ester transfer protein inhibitors)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:802732 HCAPLUS
DOCUMENT NUMBER: 141:289098
TITLE: Use of interferon-β for treating and for preventing Alzheimers disease, Creutzfeld-Jakob disease or Gerstmann-Straeussler-Scheinker disease
INVENTOR(S): Grimaldi, Luigi
PATENT ASSIGNEE(S): Ares Trading SA, Switz.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004082706	A2	20040930	WO 2004-EP50316	20040317

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-100716 A 20030319

AB The invention relates to the use of Interferon-β (IFN -β) for treating and for preventing Alzheimers disease (AD), Creutzfeld-Jakob disease (CJD) or Gerstmann-Straeussler-Scheinker disease (GSSD). It further relates to the use of IFN-β in combination with an Alzheimer's disease treating agent for treating and/or preventing Alzheimer's disease. The use of IFN-β in combination with a cholinesterase inhibitor for treating and/or preventing early-onset Alzheimer's disease is preferred.

IT **59-67-6**, Nicotinic acid, biological studies **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of interferon-β for treating and for preventing Alzheimers disease, Creutzfeld-Jakob disease or Gerstmann-Straeussler-Scheinker disease)

L24 ANSWER 4 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:648315 HCAPLUS

DOCUMENT NUMBER: 141:179622
TITLE: Controlled release pharmaceutical compositions containing polymers
INVENTOR(S): Kannan, Muthaiyyan Esakki; Krishnan, Anandi; Sapre, Beena Amol; Shah, Chitra; Patil, Atul
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004066910	A2	20040812	WO 2004-IB274	20040126
WO 2004066910	C1	20041007		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
US 2004185097	A1	20040923	US 2004-762180	20040121
PRIORITY APPLN. INFO.:			IN 2003-MU130 A	20030131
			US 2003-517589P P	20031105

AB A solid controlled release pharmaceutical composition suitable comprises a drug, a primary release-modifying agent, a secondary release-modifying agent and an auxiliary release-modifying agent, which are present in amts. that synergistically extend the release of the active ingredient. Thus, tablets contained nicotinic acid 500.00, PEG (mol. weight 4,000,000) 170.0, retrograde starch 40.00, lactose monohydrate 30.00, talc 5.00, and Mg stearate 5.00 mg, and water qs.

IT **59-67-6**, **Niacin**, biological studies **98-92-0**, Nicotinamide **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)

L24 ANSWER 5 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:615286 HCAPLUS
DOCUMENT NUMBER: 141:235399
TITLE: Medical lipid-regulating therapy: Current evidence, ongoing trials and future developments
AUTHOR(S): Evans, Marc; Roberts, Aled; Davies, Steve; Rees, Alan
CORPORATE SOURCE: Department of Metabolic Medicine, Diabetes and Endocrinology, University of Wales College of Medicine, Cardiff, UK
SOURCE: Drugs (2004), 64(11), 1181-1196
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Coronary heart disease (CHD) is a major cause of morbidity and mortality worldwide. Elevated low d. lipoprotein-cholesterol (LDL-C) and reduced high d. lipoprotein-cholesterol (HDL-C) levels are well recognized CHD risk factors, with recent evidence supporting the benefits of intensive LDL-C reduction on CHD risk. Such observations suggest that the most recent National Cholesterol Education Program Adult Treatment Panel III guidelines, with LDL-C targets of 2.6 mmol/L, may result in under-treatment of a significant number of patients and form the basis for the proposed new joint European Societies treatment targets of 2 and 4 mmol/L, resp., for LDL and total cholesterol. HMG-CoA reductase

inhibitors (statins) reduce LDL-C by inhibiting the rate-limiting step in cholesterol biosynthesis and reduced CHD event rates in primary and secondary prevention trials. The magnitude of this effect is not fully accounted for by LDL-C reduction alone and may relate to effects on other lipid parameters such as HDL-C and apolipoproteins B and A-I, as well as addnl. anti-inflammatory effects. With increasing focus on the benefits of intensive cholesterol reduction new, more efficacious statins are being developed. Rosuvastatin is a potent, hydrophilic enantiomeric statin producing redns. in LDL-C of up to 55%, with about 80% of patients reaching European LDL-C treatment targets at the 10 mg/day dosage. The Heart Protection Study (HPS) demonstrated that LDL-C reduction to levels as low as 1.7 mmol/L was associated with significant clin. benefit in a wide range of high-risk individuals, including patients with type 2 diabetes mellitus, or peripheral and cerebrovascular disease, irresp. of baseline cholesterol levels, with no apparent lower threshold for LDL-C with respect to risk. Various large endpoint trials, including Treating to New Targets (TNT) and Study of Effectiveness of Addnl. redns. in Cholesterol and Homocysteine (SEARCH) will attempt to further address the issue of optimal LDL-C reduction At low LDL-C levels, HDL-C becomes an increasingly important risk factor and is the primary lipid abnormality in over half of CHD patients, with the **Fenofibrate** Intervention and Event Lowering in Diabetes (FIELD) study set to assess the effect of raising HDL-C on cardiovascular events in patients with low HDL-C and LDL-C levels below 3 mmol/L. A variety of agents are being developed, which affect both LDL-C and HDL-C metabolism, including inhibitors of acyl-CoA-cholesterol acyl transferase, microsomal transfer protein and cholesterol ester transfer protein, as well as specific receptor agonists. Ezetimibe is a selective cholesterol absorption inhibitor, which produces redns. in LDL-C of up to 25 and 60% reduction in chylomicron cholesterol content with a 10 mg/day dosage. A 1 mmol/L reduction in LDL-C results in a 25% reduction in cardiovascular risk, independent of baseline LDL-C levels. Growing evidence supports the concept that lower is better for LDL-C and that increasing HDL-C represents an important therapeutic target. Furthermore, there is growing appreciation of the role of inflammation in atherogenesis. Consequently, increasing nos. of people should receive lipid-regulating therapy with the development of newer agents offering potential mechanisms of optimizing lipid profiles and thus risk reduction In addition, the pleiotropic anti-inflammatory effects of lipid lowering therapy may provide further risk reduction

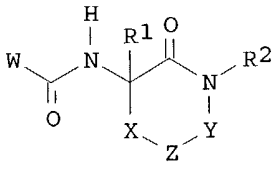
IT **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical lipid-regulating therapy)

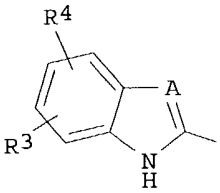
REFERENCE COUNT: 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 6 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:589248 HCAPLUS
DOCUMENT NUMBER: 141:140474
TITLE: Triglyceride and triglyceride-like prodrugs of glycogen phosphorylase inhibiting compounds
INVENTOR(S): Sher, Philip M.; Ellsworth, Bruce A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 43 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004142938 A1 20040722 US 2003-712823 20031113
PRIORITY APPLN. INFO.: US 2002-426465P P 20021114
OTHER SOURCE(S): MARPAT 141:140474
GI





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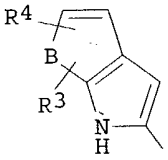

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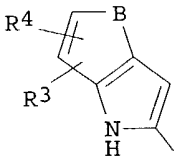


= W3

AB Prodrugs of glycogen phosphorylase inhibiting compds. are provided, said prodrug compds., G(-O2CR')m(-OH)n(-O2C(CH2)pCH3)q [G = branched or straight C3-5-carbon chain and (-O2CR'), (-OH) and (-O2C(CH2)pCH3) are attached to any available carbon atom along G; m = 1 - 4; n = 0 - 3; p = 0 - 16; q = 0 - 3; where m + n + q = 3 or 4; and -O2CR' is a fragment of a compound I wherein W = W1, W2, W3; X = O, S, SO2, CHR5, , CHR5O, CHR5S, CHR5SO2, CHR5CO, CH2CHR5; Y = bond, CHR6; Z = aryl, heteroaryl; R1 =H, alkyl, alkenyl; R2 = H, alkyl, aryl, arylalkyl, heteroarylalkyl, alkenyl; R3, R4 = H, halo, CF3, CN, alkyl, alkoxy; R5, R6 = H, alkyl, aryl, alkenyl, CN, CN4R9A (tetrazole), CO2R9A, CONR9AR9B, CONR9AOR9B; A = CH, N; B = O, S; wherein R1, R2, R5, R6, R7, R8 = alkyl, aryl, alkenyl, arylalkyl,heteroarylalkyl, alkoxy, aryloxy and each may be substituted with 1 - 3 hydrogen bonding groups]. Thus, 3-[(5-chloroindolecarbonyl)amino]-3,4-dihydrocarbostyril I (R1 = R2 = H, W = 5-chloroindole, X = CH2, YZ = benzo) was prepared from 3-amino-3,4-dihydrocarbostyril via acylation with 5-chloroindolecarboxylic acid resin-bound 2,3,5,6-tetrafluorophenyl ester. Further provided are pharmaceutical compns. and methods for treating diabetes and related diseases employing compds. above, either alone or in combination with another therapeutic agent.

IT **59-67-6D**, Nicotinic acid, derivative **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**, Visastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(companion therapeutic agent (lipid-lowering); preparation of triglyceride and triglyceride-like prodrugs of glycogen phosphorylase inhibiting compds.)

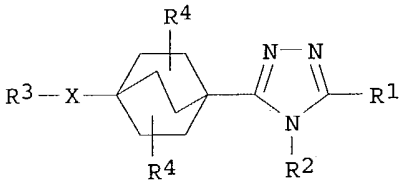
L24 ANSWER 7 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:550802 HCAPLUS
DOCUMENT NUMBER: 141:106490
TITLE: Preparation of 2-(bicyclo[2.2.2]octan-1-yl)-1,2,4-triazole derivatives as inhibitors of 11-beta-hydroxysteroid dehydrogenase-1

INVENTOR(S): Waddell, Sherman T.; Santorelli, Gina M.; Maletic, Milana M.; Leeman, Aaron H.; Gu, Xin; Graham, Donald W.; Balkovec, James M.; Aster, Susan D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 76 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004133011	A1	20040708	US 2003-739716	20031218
WO 2004058741	A1	20040715	WO 2003-US40127	20031216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004058730	A2	20040715	WO 2003-US40128	20031216
WO 2004058730	A3	20040902		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
US 2002-435074P P 20021220
US 2003-458592P P 20030328
US 2003-503410P P 20030916

OTHER SOURCE(S): MARPAT 141:106490
GI



I

AB Ther title compds. (I) [X = O, S(O)p, NR6, CONR6, NR6CO, NR6CONR6, NR6SO2, SO2NR6, NR6CO2, O2CNR6, CO2, O2C [wherein p = 0-2; R6 = C1-8 alkyl, (CH2)n-aryl, (CH2)n-heteroaryl, (CH2)n-C3-7 cycloalkyl; wherein alkyl, aryl, heteroaryl, and cycloalkyl are optionally substituted; or two R6 groups together with the atom to which they are attached form a 5- to

8-membered mono or bicyclic ring system optionally containing an addnl. heteroatom selected from O, S, and NC1-4 alkyl]; R1 = arylcarbonyl, (CH2)n-aryl, (CH2)n- heteroaryl, in which aryl and heteroaryl are optionally substituted (wherein n = 0-2); R2 = H, C1-8 alkyl, C2-6 alkenyl, and (CH2)n-C3-6 cycloalkyl, in which alkyl, alkenyl, and cycloalkyl are optionally substituted; R4 = H, halogen, HO, oxo, C1-3 alkyl, C1-3 alkoxy; R3 = H, C1-10 alkyl, C2-10 alkenyl, (CH2)n-C3-6 cycloalkyl, (CH2)n-aryl, and (CH2)n-heteroaryl, (CH2)n-heterocyclyl, in which alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl are optionally unsubstituted] are prepared These compds. are selective inhibitors of the 11β-hydroxysteroid dehydrogenase-1 (no data). They are useful for the treatment of diabetes, such as noninsulin-dependent diabetes (NIDDM), hyperglycemia, obesity, insulin resistance, dyslipidemia, hyperlipidemia, hypertension, metabolic syndrome X, lipid disorder, atherosclerosis, and other symptoms associated with NIDDM. Thus, chlorination of N-methyl-4-pentylbicyclo[2.2.2]octane-1-carboxamide by oxalyl chloride in CH2Cl2 at room temperature for 2 h gave N-methyl-4-pentylbicyclo[2.2.2]octane-1-carboximidoyl chloride which was condensed with 5-[4-(benzyloxy)-2-methoxyphenyl]-2H-tetrazole in toluene at 120° for 9 h under refluxing to give 3-[4-(benzyloxy)-2-methoxyphenyl]-4-methyl-5-(4-pentylbicyclo[2.2.2]oct-1-yl)-4H-1,2,4-triazole (II). Hydrogenolysis of II over 10% Pd-C in MeOH for 19 h gave 3-methoxy-4-[4-methyl-5-(4-pentylbicyclo[2.2.2]oct-1-yl)-4H-1,2,4-triazol-3-yl]phenol.

IT **59-67-6**, Nicotinic acid, biological studies **147098-20-2**, ZD-4522, calcium salt
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of 2-(bicyclo[2.2.2]octan-1-yl)-1,2,4-triazole derivs. as selective inhibitors of 11-beta-hydroxysteroid dehydrogenase-1 for treating diabetes, hyperglycemia, obesity, atherosclerosis, etc.)

L24 ANSWER 8 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:533962 HCAPLUS
DOCUMENT NUMBER: 141:82335
TITLE: Human glucagon-like-peptide-1 mimics and their antidiabetic effects
INVENTOR(S): Natarajan, Sesha Iyer; Mapelli, Claudio; Bastos, Margarita M.; Bernatowicz, Michael; Lee, Ving; Ewing, William R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 273,975.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004127423	A1	20040701	US 2003-419399	20030421
US 2003195157	A1	20031016	US 2002-273975	20021018
WO 2004094461	A2	20041104	WO 2004-US12374	20040421

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,

SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-342015P P 20011018
US 2002-273975 A2 20021018
US 2003-419399 A 20030421

AB The invention discloses human glucagon-like peptide-1 (GLP-1) peptide mimics that mimic the biol. activity of the native GLP-1 peptide and thus are useful for the treatment or prevention of diseases or disorders associated with GLP activity. Further, the invention provides novel, chemical modified peptides that not only stimulate insulin secretion in type II diabetics, but also produce other beneficial insulinotropic responses. These synthetic peptide GLP-1 mimics exhibit increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral administration.

IT **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)

L24 ANSWER 9 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:392331 HCAPLUS
DOCUMENT NUMBER: 140:406798
TITLE: Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors
INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 875,155, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004092573	A1	20040513	US 2003-602752	20030624
US 6812345	B2	20041102		
US 2002013334	A1	20020131	US 2001-875155	20010606

PRIORITY APPLN. INFO.: US 2000-211595P P 20000615
US 2001-875155 B2 20010606

OTHER SOURCE(S): MARPAT 140:406798
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = O, S, SO, SO2, NR7; Z = HOCHCH2CH(OH)CH2CO2R3, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H, alkyl, metal ion; R4 = H, halo, CF3, etc.; R7 = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R9, R10 = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). A multistep synthesis of II is reported.

IT **59-67-6**, **Niacin**, biological studies **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**, Rosuvastatin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

IT **59-67-6D**, Nicotinic acid, derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

L24 ANSWER 10 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:384070 HCAPLUS
DOCUMENT NUMBER: 140:417144
TITLE: Quantification of the N-desmethyl metabolite of rosuvastatin in human plasma by automated SPE followed by HPLC with tandem MS detection
AUTHOR(S): Hull, Caroline K.; Martin, Paul D.; Warwick, Michael J.; Thomas, Elizabeth
CORPORATE SOURCE: Quintiles Scotland Limited, Riccarton, Edinburgh, EH14 4AP, UK
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2004), 35(3), 609-614
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A selective, accurate and precise assay was developed for the quantification in human plasma of the N-desmethyl metabolite of the 3-hydroxy-3-methylglutaryl CoA (HMG-CoA) reductase inhibitor rosuvastatin. The assay employing automated SPE followed by HPLC with pos. ion electrospray tandem MS (HPLC-MS/MS) was validated. The standard curve range for N-desmethyl rosuvastatin in human plasma was 0.5-30 ng/mL with 0.5 ng/mL being the limit of quantification. Plasma samples were mixed 1:1 with sodium acetate buffer (pH 4.0; 0.1 M) soon after separation from red blood cells. N-Desmethyl rosuvastatin was stable in plasma:buffer at room temperature for 24 h and at -70° for 12 mo. The assay was applied successfully to the quantification of N-desmethyl rosuvastatin in human plasma following administration of rosuvastatin.
IT **371775-74-5**
RL: ANT (Analyte); ANST (Analytical study)
(quantification of N-desmethylrosuvastatin in human plasma by automated SPE followed by HPLC with tandem MS detection)
IT **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quantification of N-desmethylrosuvastatin in human plasma by automated SPE followed by HPLC with tandem MS detection)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 11 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:368874 HCAPLUS
DOCUMENT NUMBER: 140:357672
TITLE: Preparation of glycinenitrile-based inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Magnin, David R.; Hamann, Lawrence G.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037181	A2	20040506	WO 2003-US33385	20031021
WO 2004037181	A3	20041021		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-420603P P 20021023
OTHER SOURCE(S): MARPAT 140:357672

AB Glycinenitrile derivs. R4NHCHR3CONR2CHR1CN [R1 is H, alk(en)(yn)yl or (cyclo)alk(en)yl; R2 is (un)substituted alk(en)(yn)yl, (cyclo)alk(en)yl or arylalk(en)(yn)yl; R3 is group given for R2 or cycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, (hetero)aryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl, which may be substituted; R4 is H or can combine with R3 to form a 4- to 5-membered heterocyclic ring] were prepared for use in pharmaceutical compns. for the treatment of diabetes and related diseases. Thus, (S)-H2NCH(Ad)CONEtCH2CN was prepared by condensation of (S)-Boc-NHCH(Ad)CO2H (Boc = tert-butoxycarbonyl) with EtNHCH2CN (syntheses given), followed by deprotection using trifluoroacetic acid.

IT **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (lipid-lowering agent; preparation of glycinenitrile amino acid derivs. as inhibitors of dipeptidyl peptidase IV)

IT **287714-41-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (lipid-lowering agent; rosuvastatin; preparation of glycinenitrile amino acid derivs. as inhibitors of dipeptidyl peptidase IV)

L24 ANSWER 12 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:364075 HCAPLUS
DOCUMENT NUMBER: 141:388103
TITLE: The effect of gemfibrozil on the pharmacokinetics of rosuvastatin
AUTHOR(S): Schneck, Dennis W.; Birmingham, Bruce K.; Zalikowski, Julie A.; Mitchell, Patrick D.; Wang, Yi; Martin, Paul D.; Lasseter, Kenneth C.; Brown, Colin D. A.; Windass, Amy S.; Raza, Ali
CORPORATE SOURCE: AstraZeneca, Miami, FL, USA
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2004), 75(5), 455-463
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Coadministration of statins and gemfibrozil is associated with an increased risk for myopathy, which may be due in part to a pharmacokinetic interaction. Therefore the effect of gemfibrozil on rosuvastatin pharmacokinetics was assessed in healthy volunteers. Rosuvastatin has been shown to be a substrate for the human hepatic uptake transporter organic anion transporter 2 (OATP2). Inhibition of this transporter could

increase plasma concns. of rosuvastatin. The effect of gemfibrozil on rosuvastatin uptake by cells expressing OATP2 was also examined Methods: In a randomized, double-blind, 2-period crossover trial, 20 healthy volunteers were given oral doses of gemfibrozil, 600 mg, or placebo twice daily for 7 days. On the fourth morning of each dosing period, a single oral dose of rosuvastatin, 80 mg, was coadministered. Plasma concns. of rosuvastatin, N-desmethyl rosuvastatin, and rosuvastatin-lactone were measured. In addition, the effect of gemfibrozil on the uptake of radiolabeled rosuvastatin by OATP2-transfected Xenopus oocytes was studied. Results: Gemfibrozil increased the rosuvastatin area under the plasma concentration-time curve from time 0 to the time of the last quantifiable concentration [AUC(0-t)] 1.88-fold (90% confidence interval, 1.60-2.21) and the maximum observed rosuvastatin plasma concentration (Cmax) 2.21-fold (90% confidence interval, 1.81-2.69) compared with placebo. N-desmethyl rosuvastatin AUC(0-t) and Cmax decreased by 48% and 39%, resp. Pharmacokinetics of rosuvastatin-lactone was unchanged. The in vitro results indicate that the maximum gemfibrozil inhibition of rosuvastatin OATP2-mediated uptake was 50%; the inhibition constant for the inhibitory process was 4.0±1.3 μmol/L. Conclusions. Gemfibrozil increased rosuvastatin plasma concns. approx. 2-fold, which is similar to the effect of gemfibrozil on pravastatin, simvastatin acid, and lovastatin acid plasma concns. and substantially less than the effect observed for cerivastatin. Gemfibrozil inhibition of OATP2-mediated rosuvastatin hepatic uptake may contribute to the mechanism of the drug-drug interaction. Care is warranted when gemfibrozil is coadministered with rosuvastatin and other statins.

IT **371775-74-5**, N-Desmethyl rosuvastatin
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(gemfibrozil decreased AUC, Cmax of N-desmethyl rosuvastatin in healthy human and inhibit OATP2 mediated rosuvastatin uptake in Xenopus oocyte)

IT **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gemfibrozil increased rosuvastatin AUC, plasma concentration in healthy human indicating care should be taken when gemfibrozil is coadministered with rosuvastatin)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:336126 HCAPLUS
DOCUMENT NUMBER: 141:21194
TITLE: Is high-density lipoprotein the protector of the cardiovascular system?
AUTHOR(S): Barter, P.
CORPORATE SOURCE: The Heart Research Institute, Sydney, Australia
SOURCE: European Heart Journal Supplements (2004), 6(Suppl. A), A19-A22
CODEN: EHJSFT; ISSN: 1520-765X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Low high-d. lipoprotein (HDL-C) cholesterol is a powerful predictor of risk for coronary heart disease (CHD), and raising HDL-C reduces CHD risk, with available data indicating a 1% decrease in risk with each 1% increase in HDL-C. Both epidemiol. and intervention studies have shown that HDL is predictive of risk independent of low-d. lipoprotein cholesterol. In treatment trials, both fibrates and statins have been shown to reduce risk in patients with low HDL-C. Statins reduce risk across all HDL-C levels from low to high, whereas fibrates appear to

have benefits limited to low HDL-C in the context of the metabolic syndrome. The primary management component of increasing HDL-C is lifestyle intervention focusing on diet, exercise and smoking cessation. Drug options for raising HDL-C include **niacin** (+10-30%), fibrates (+5-25%) and statins (+3-12%). **Niacin** is poorly tolerated. **Fenofibrate** may pose advantages over gemfibrozil among fibrates. Findings in the large-scale Statin Therapies for Elevated Lipid Levels compared Across dose ranges to Rosuvastatin (STELLAR) trial indicate that rosuvastatin has the best HDL-C raising effect among statins. Selection of therapy requires consideration of the individual patient's overall risk profile.

IT **59-67-6**, **Niacin**, biological studies
RL: BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(LDL- and HDL-cholesterol and statins in scardiovascular disease)

IT **49562-28-9**, **Fenofibrate 287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LDL- and HDL-cholesterol and statins in scardiovascular disease)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

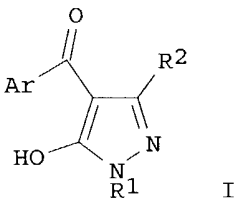
L24 ANSWER 14 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:333698 HCAPLUS
DOCUMENT NUMBER: 140:357333
TITLE: Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders
INVENTOR(S): Semple, Graeme; Shin, Young Jun
PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033431	A2	20040422	WO 2003-US31509	20031002
WO 2004033431	A3	20040729		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-416193P P 20021004
US 2002-417120P P 20021007

OTHER SOURCE(S): MARPAT 140:357333
GI



I

AB Title compds. [I; R1 = alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, benzyl, optionally substituted with ≥1 halo, OH, cyano, NO2, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl, alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalklcylsulfonyl, alkylureyl, arylureyl; R2 = H, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, PhCH2, Ph, heteroaryl, optionally substituted with ≥1 halo, OH, cyano, nitro, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl, alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfmyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylureyl or arylureyl groups; Ar = (substituted) pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl], were prepared for the treatment of metabolic-related disorders, including dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, type 2 diabetes, Syndrome-X and the like (no data). Thus, nicotinyl chloride, 2-methyl-5-propyl-2,4-dihydropyrazol-3-one, and Ca(OH)2 were heated at 90° in dioxane for 2 h. to give (5-hydroxy-1-methyl-3-propyl-1H-pyrazol-4-yl)pyridin-3-ylmethanone. I may be used in combination with other active agents such α-glucosidase inhibitors, aldose reductase inhibitors, biguanides, HMG-CoA reductase inhibitors, squalene synthesis inhibitors, fibrates, LDL catabolism enhancers, angiotensin converting enzyme inhibitors, and insulin secretion enhancers.

IT **637-07-0**, **Clofibrate 882-09-7**, Clofibric acid
41859-67-0, **Bezafibrate 49562-28-9**,
Fenofibrate 52214-84-3, **Ciprofibrate**
54504-70-0, Theofibrate **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of aroylhydroxypyrazoles for treatment of metabolic disorders)

L24 ANSWER 15 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:316924 HCAPLUS
DOCUMENT NUMBER: 141:374557
TITLE: Rosuvastatin-Induced Arrest in Progression of Renal Disease
AUTHOR(S): Vidt, Donald G.; Cressman, Michael D.; Harris, Susan; Pears, John S.; Hutchinson, Howard G.
CORPORATE SOURCE: Cleveland Clinic Foundation, Cleveland, OH, USA
SOURCE: Cardiology (2004), 102(1), 52-60
CODEN: CAGYAO; ISSN: 0008-6312
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Preclin. and limited clin. data suggest that statins decrease the progressive decline in renal function that occurs in patients with renal disease. Pooled anal. of data obtained from a population of hyperlipidemic patients enrolled in the rosuvastatin (Crestor) clin. development program permitted assessment of its effects on renal function both early and later in the course of treatment. Study participants were

initially included in controlled clin. trials that evaluated the lipid-lowering efficacy and safety of rosuvastatin when compared with placebo or other lipid-lowering agents (i.e., atorvastatin, simvastatin, pravastatin, cholestyramine, **fenofibrate** or extended-release **niacin**). The median duration of treatment with the various doses of statins in these trials was approx. 8 wk. Following completion of a controlled clin. trial, patients were permitted to enter an open-label extension trial and received rosuvastatin treatment. These data permitted assessment of renal function in a diverse group of over 10,000 patients who received rosuvastatin in its recommended dose range (5-40 mg) for up to 3.8 yr. Mean serum creatinine concns. were lower when compared with baseline both early and later in the course of rosuvastatin treatment. In contrast, no change in mean serum creatinine was observed with placebo. Mean glomerular filtration rates (GFR) predicted from the Modification of Diet in Renal Disease (MDRD) equation were higher when compared with baseline both early and later in the course of rosuvastatin treatment. No change in GFR was observed in the placebo group. Among patients who received long-term rosuvastatin treatment (≥96 wk), GFR was unchanged or tended to increase, rather than decrease, when compared with baseline irresp. of age, gender, hypertensive or diabetic status, level of renal function (GFR ≥60 vs. <60 mL/min/1.73 m2) at entry or urine dipstick protein status prior to or during the period of treatment. These findings suggest that rosuvastatin may arrest the progression of renal disease.

IT **147098-20-2**, Crestor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HMG-CoA reductase inhibitor rosuvastatin induced arrest in progression of chronic renal disease with reduced mean serum creatinine level and increased mean glomerular filtration rate in hyperlipidemic patient)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 16 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:287775 HCAPLUS
DOCUMENT NUMBER: 140:309387
TITLE: Oral pharmaceutical compositions of **fenofibrate** having high bioavailability
INVENTOR(S): Miriyala, Gowri Shankar; Singla, Ajay Kumar; Malik, Rajiv
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India; Roy, Sunilendu Bhushan
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004028506	A1	20040408	WO 2003-IB4162	20030924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2002-DE961 A 20020924

AB The present invention relates to oral pharmaceutical compns. of **fenofibrate** having high bioavailability with improved dissoln. and methods for providing the pharmaceutical compns. The oral pharmaceutical composition of **fenofibrate** include an inert hydro-insol. carrier having one or more one layers that include **fenofibrate** in a micronized form, one or more hydrophilic polymers, and one or more surfactants. The composition may have a dissoln. profile of at least about 10% in about 5 min, about 20% in about 10 min, about 50% in about 20 min and about 75% in about 30 min, as measured using the rotating blade method at 75 rpm according to the European Pharmacopoeia in a dissoln. medium constituted by water with 2% by weight of Polysorbate 80 or with 0.025M sodium lauryl sulfate.

IT **59-67-6**, **Niacin**, biological studies **49562-28-9**, **Fenofibrate 287714-41-4**, Rosuvastatin
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(oral pharmaceutical compns. of **fenofibrate** having high bioavailability)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 17 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:281558 HCAPLUS
DOCUMENT NUMBER: 141:343223
TITLE: Rosuvastatin and **fenofibrate** alone and in combination in type 2 diabetes patients with combined hyperlipidemia
AUTHOR(S): Durrington, Paul N.; Tuomilehto, Jaakko; Hamann, Andreas; Kallend, David; Smith, Karen
CORPORATE SOURCE: Manchester Royal Infirmary, Department of Medicine, University of Manchester, Manchester, M13 9WL, UK
SOURCE: Diabetes Research and Clinical Practice (2004), 64(2), 137-151
CODEN: DRCPE9; ISSN: 0168-8227
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to evaluate the effects of rosuvastatin and **fenofibrate** alone and in combination in type 2 diabetes associated with combined hyperlipidemia. A total of 216 patients with total cholesterol ≥200 mg/dL (≥5.17 mmol/l) and triglycerides ≥200 and <800 mg/dL (≥2.26 and <9.03 mmol/l) were randomized to one of two placebo groups, rosuvastatin 5 mg or rosuvastatin 10 mg for 6 wk (fixed-dose phase). During the subsequent 18-wk dose-titration phase, one placebo group received titrated rosuvastatin 10, 20 and 40 mg (placebo/rosuvastatin); one placebo group received titrated **fenofibrate** 67 mg once, twice and three times daily (placebo/**fenofibrate**); and patients receiving 5 or 10 mg rosuvastatin received titrated **fenofibrate** as above (rosuvastatin 5 mg/**fenofibrate** and rosuvastatin 10 mg/**fenofibrate** groups). Doses were increased at 6-wk intervals if low-d. lipoprotein (LDL) cholesterol remained >50 mg/dL (>1.3 mmol/l). At 24 wk, the placebo/rosuvastatin group and placebo per **fenofibrate** group had triglyceride redns. of 30.3% vs. 33.6%, resp. (P=NS), and LDL cholesterol was reduced by 46.7% in the rosuvastatin group and increased by 0.7% in the **fenofibrate** group (P<0.001). The triglyceride reduction in the rosuvastatin 10 mg/**fenofibrate** group (47.1%) was significantly greater than in the placebo/rosuvastatin group (P=0.001), with no significant differences in other lipid measures found between these two groups. No significant differences in effect on high-d. lipoprotein (HDL) were observed among treatment groups. In the fixed-dose phase, rosuvastatin 5 and 10 mg reduced triglycerides by 24.5 and 29.5%, resp., and decreased

LDL cholesterol by 40.7 and 45.8%, resp. All treatments were well tolerated. These results indicated that rosuvastatin produces marked redns. in triglycerides and LDL cholesterol when used alone or in combination with **fenofibrate** in type 2 diabetes patients with elevated cholesterol and triglyceride levels and may constitute a valuable treatment option in the diabetic population.

IT **49562-28-9**, **Fenofibrate 287714-41-4**,
Rosuvastatin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rosuvastatin alone or in combination with **fenofibrate** was well tolerated, reduced triglyceride and LDL cholesterol in type 2 diabetic patients with combined hyperlipidemia)

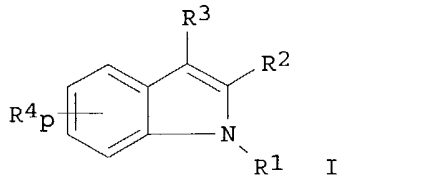
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 18 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:203809 HCAPLUS
DOCUMENT NUMBER: 140:253443
TITLE: Preparation of indoles having aryloxyalkanoic or arylalkanoic acid substituents as PPARγ agonists or partial agonists having anti-diabetic activity
INVENTOR(S): Acton, John J., III; Debenham, Sheryl D.; Liu, Kun; Meinke, Peter T.; Wood, Harold B.; Black, Regina M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020409	A1	20040311	WO 2003-US27156	20030827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2002-406741P P 20020829
US 2003-440672P P 20030117

OTHER SOURCE(S): MARPAT 140:253443
GI



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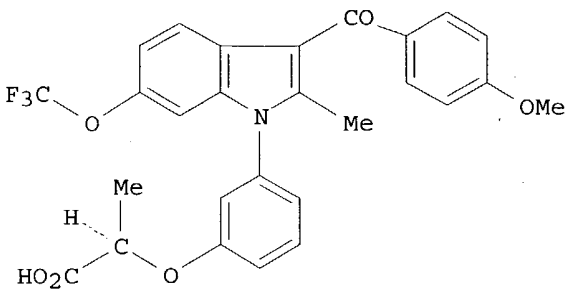


II

AB Indoles having aryloxyalkanoic acid or arylalkanoic acid substituents (shown as I; variables defined below; e.g. II) are agonists or partial agonists of PPARγ and are useful in the treatment and control of hyperglycemia that is symptomatic of type 2 diabetes, as well as dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, and obesity that are often associated with type 2 diabetes. For I: R1 = -X-Aryl-Y-Z, and -X-Heteroaryl-Y-Z, wherein Aryl and Heteroaryl are (un)substituted with 1-3 A; Aryl is Ph or naphthyl; Heteroaryl is a monocyclic or fused bicyclic aromatic ring structure containing 1-4 heteroatoms = N, O, and S(O)n, wherein the monocyclic ring or each ring of the bicyclic ring structure is a 5-6 membered ring; X = a bond, CH2, CHMe, CMe2, and C3-C6cycloalkylidene; Y = -CH:CH-, -CH(OH)CH(OH)-, -OCR7R8-, -SCR7R8-, and -CH2CR5R6-; Z = -CO2H and tetrazole; A = C1-4 alkyl, C1-4 alkenyl, -OC1-4 alkyl, and halogen, wherein alkyl, alkenyl, and -Oalkyl are each (un)substituted with 1-5 halogens. R2 is C1-C4 alkyl, which is (un)substituted with 1-5 halogens; R3 = benzisoxazolyl, benzisothiazolyl, benzopyrazolyl, Aryl, -C(O)Aryl, -C(O)Heteroaryl, -OAryl, OHeteroaryl, -S(O)nAryl, and -S(O)nHeteroaryl, wherein R3 is (un)substituted with 1-3 halogen, C1-3alkyl, -OC1-3alkyl, and -SC1-3 alkyl, wherein C1-3alkyl, -OC1-3alkyl, and-SC1-3alkyl are (un)substituted with 1-5 halogens; each R4 is optionally = H, halogen, C1-C5 alkyl and -OC1-C5 alkyl, wherein C1-C5 alkyl and -OC1-C5 alkyl are (un)substituted with 1-5 halogens; n = 0-2; and p = 1-3; addnl. details are given in the claims. Compds. I have EC50 = 1-3000 nM in Gal-4 hPPAR transactivation assays (no data for individual compds. are given). Although the methods of preparation are not claimed, 32 example prepns. are included. For example, II was prepared in 5 steps starting with N-arylation of 2-methyl-6-trifluoromethoxyindole by 3-bromoanisole to give 1-(3-methoxyphenyl)-2-methyl-6-trifluoromethoxyindole, followed by ether cleavage, followed by substitution at the 3-position with 4-methoxybenzoyl chloride, followed by ether formation with (S)-Et lactate and finally base hydrolysis of the ester functionality.

IT **59-67-6**, Nicotinic acid, biological studies **147098-20-2**, ZD-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of indoles having aryloxyalkanoic or arylalkanoic acid substituents as PPARγ agonists or partial agonists having anti-diabetic activity)

IT **59-67-6D**, Nicotinic acid, salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(codrugs; preparation of indoles having aryloxyalkanoic or arylalkanoic acid substituents as PPARγ agonists or partial agonists having anti-diabetic activity)

IT **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of indoles having aryloxyalkanoic or arylalkanoic acid substituents as PPARγ agonists or partial agonists having anti-diabetic activity)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 19 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:203619 HCAPLUS
DOCUMENT NUMBER: 140:253441
TITLE: Preparation of indoles having aryloxyalkanoic or arylalkanoic acid substituents as PPARγ agonists or partial agonists having anti-diabetic activity
INVENTOR(S): Acton, John J., III; Meinke, Peter T.; Wood, Harold B.; Black, Regina M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

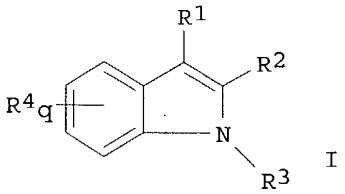
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019869	A2	20040311	WO 2003-US26679	20030828
WO 2004019869	A3	20040624		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-406737P P 20020829
US 2003-440741P P 20030117

OTHER SOURCE(S): MARPAT 140:253441
GI



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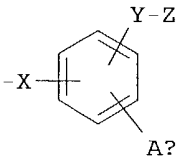

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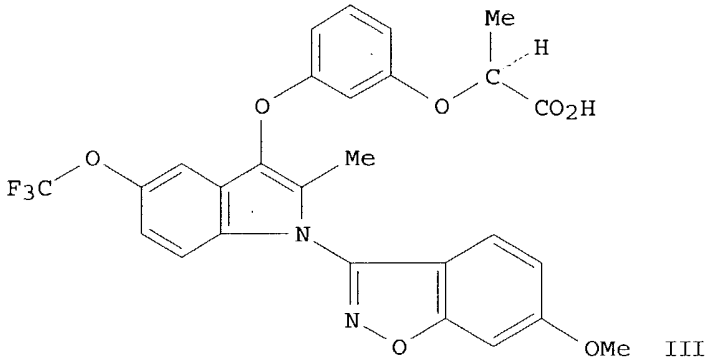


III

AB Indoles having aryloxyalkanoic acid substituents or arylalkanoic acid substituents are agonists or partial agonists of PPAR gamma and are useful in the treatment and control of hyperglycemia that is symptomatic II diabetes, as well as dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, and obesity that are often associated with type 2 diabetes. Indoles having aryloxyalkanoic acid or arylalkanoic acid substituents (shown as I; variables defined below; e.g. III) are agonists or partial agonists of PPARγ and are useful in the treatment and control of hyperglycemia that is symptomatic of type 2 diabetes, as well as dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, and obesity that are often associated with type 2 diabetes. Compds. I have EC50 = 1-3000 nM in Gal-4 hPPAR transactivation assays (no data for individual compds. are given). For I: R1 is II wherein X = a bond, O, S(O)n, CO, CH2, CHMe, CMe2, and C3-6cycloalkylidene; Y = -CH:CH-, -CH(OH)CH(OH)-, -OCR7R8-, -SCR7R8-, and -CH2CR5R6-; Z = -CO2H and tetrazole; A = H, C1-4 alkyl, C1-4 alkenyl, -O1-4-alkyl, and halogen, wherein alkyl, alkenyl, and Oalkyl are (un)substituted with 1-5 halogens. R5, R6, R7, and R8 = H, halogen, C1-C5 alkyl, OC1-C5 alkyl, C2-C5 alkenyl, OC2-C5 alkenyl, C3-6 cycloalkyl, (CH2)0-2phenyl, -O(CH2)0-2phenyl and CO2H, wherein C1-C5 alkyl, OC1-C5 alkyl, C2-C5 alkenyl, OC2-C5 alkenyl, C3-6 cycloalkyl, and Ph are (un)substituted with 1-5 halogens, and C3-6 cycloalkyl and Ph are further (un)substituted with 1-3 C1-C3 alkyl and OC1-C3 alkyl, said C1-C3 alkyl and OC1-C3 alkyl being (un)substituted with 1-3 halogens; or R7 and R8 may be connected to form a C3-C6 cycloalkyl group, said C3-C6 cycloalkyl being (un)substituted with 1-3 halogens; or, when Y is OCR7R8, R8 may optionally be a 1-2-C bridge connected to the Ph ring at the position ortho to Y, thereby yielding a 5 or 6-membered heterocyclic ring fused to the Ph ring. R2 is C1-C4 alkyl, which is (un)substituted with 1-5 halogens; R3 = 3-benzisoxazolyl, 3-benzisothiazolyl, and 3-benzpyrazolyl, wherein R3 is (un)substituted with 1-3 halogen, C1-3alkyl, and OC1-3alkyl, wherein C1-3alkyl and OC1-3alkyl are (un)substituted with 1-5 halogens; each R4 = halogen, C1-C3 alkyl, and OC1-C5 alkyl, wherein C1-C3 alkyl and OC1-C5 alkyl are (un)substituted with 1-5 halogens; n = 0-2; p = 0-3; and q = 0-3. Although the methods of preparation are not claimed, 11 example prepns. are included. For example, III was prepared in 8 steps starting with substitution of chloroacetone with 3-benzoyloxyphenol to give 1-(3-hydroxyphenoxy)-2-propanone followed by cyclization with

4-trifluoromethoxyphenylhydrazine hydrochloride to give 3-(3-hydroxyphenoxy)-2-methyl-5-(trifluoromethoxy)-1H-indole, followed by O-protection, followed by substitution at N with 3,6-dichloro-1,2-benzisoxazole, followed by deprotection at O, followed by etherification with iso-Bu (R)-lactate, followed by base hydrolysis of the ester functionality, followed by substitution of MeO for Cl.

IT **59-67-6**, Nicotinic acid, biological studies **147098-20-2**, ZD-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of indoles having aryloxyalkanoic or arylalkanoic acid substituents as PPARγ agonists or partial agonists having anti-diabetic activity)

IT **59-67-6D**, Nicotinic acid, salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of indoles having aryloxyalkanoic or arylalkanoic acid substituents as PPARγ agonists or partial agonists having anti-diabetic activity)

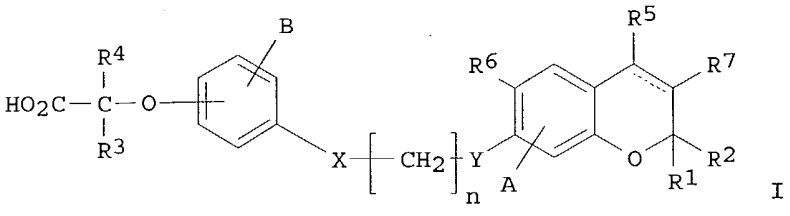
IT **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of indoles having aryloxyalkanoic or arylalkanoic acid substituents as PPARγ agonists or partial agonists having anti-diabetic activity)

L24 ANSWER 20 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:100986 HCAPLUS
DOCUMENT NUMBER: 140:157460
TITLE: PPARα-selective chromane and chromene compounds for the treatment of dyslipidemia and other lipid disorders, and preparation thereof
INVENTOR(S): Desai, Ranjit C.; Sahoo, Soumya
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004010992	A1	20040205	WO 2003-US23499	20030725

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-399518P P 20020730
OTHER SOURCE(S): MARPAT 140:157460
GI



I

AB A class of chromane and chromene compds. I [R1, R2, R4 = (un)substituted C1-3 alkyl; R3, R5, R7 = H, (un)substituted C1-3 alkyl; R6 = H, Cl, Me, CF3; A, B = H, Cl, F, Me, CF3; X, Y = O, S; n = 2, 3; dashed line = optional double bond], and pharmaceutically acceptable salts thereof, are useful as therapeutic compds., particularly in the treatment and control of hyperlipidemia, hypercholesterolemia, dyslipidemia, and other lipid disorders, and in delaying the onset of or reducing the risk of conditions and sequelae that are associated with these diseases, such as atherosclerosis. Compound preparation is included.

IT **59-67-6**, Nicotinic acid, biological studies **147098-20-2**, ZD 4522, calcium salt **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PPARα-selective chromane and chromene compds. for treatment of lipid disorders, preparation, and use with other agents)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 21 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:100946 HCAPLUS
DOCUMENT NUMBER: 140:145991
TITLE: Preparation of benzodihydrofurans as selective PPARα agonists for treating dyslipidemia and other lipid disorders
INVENTOR(S): Shi, Guo Q.; Zhang, Yong
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004010936	A2	20040205	WO 2003-US23430	20030725
WO 2004010936	A3	20040826		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-399520P P 20020730
OTHER SOURCE(S): MARPAT 140:145991
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R = (un)substituted alkyl, (CH2)0-2-cycloalkyl; R1 = Cl, F, (un)substituted alkyl, (CH2)0-2-cycloalkyl; R2 = (un)substituted thio/alkoxy, (CH2)0-3-cycloalkyl, alkyl; R3, R4 = independently H, Cl, F, (un)substituted alkyl; A, B = independently H, halo, (un)substituted alkyl, alkoxy; X, Y = independently O, S, CR3R4; n = 1-3; and their pharmaceutically acceptable salts] were prepared as selective peroxisome proliferator-activated receptors alpha (PPARα) for treating dyslipidemia and other lipid disorders (no data). For example, II was prepared by chlorination of 2-chloro-4-(2,2,2-trifluoroethoxy)phenol, etherification with 3-bromopropanol, iodination to III, etherification of 5-hydroxy-dihydrobenzofuran (preparation given) with III, and subsequent hydrolysis of the "in situ" prepared Me ester. I exhibited high agonist activity at the PPARα receptor and little or no activity at the PPARγ and PPARδ receptors (no data). Thus, I and their formulations, are useful for treating hyperlipidemia, hypercholesterolemia, dyslipidemia, and other lipid disorders, and in delaying the onset of or reducing the risk of conditions and sequelae that are associated with these diseases, such as atherosclerosis and diabetes mellitus, type II insulin-independent (no data).

IT **59-67-6D**, Nicotinic acid, salts **147098-20-2**
287714-41-4, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of benzodihydrofurans as selective PPARα agonists for treating dyslipidemia and other lipid disorders)

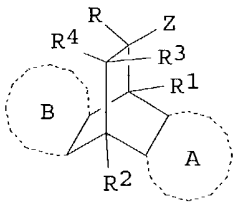
L24 ANSWER 22 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:80450 HCAPLUS
DOCUMENT NUMBER: 140:145835
TITLE: Preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of the glucocorticoid receptor
INVENTOR(S): Vaccaro, Wayne; Yang, Bingwei Vera; Kim, Soong-hoon; Huynh, Tram; Tortolani, David R.; Leavitt, Kenneth J.; Li, Wenying; Doweyko, Arthur M.; Chen, Xiao-tao; Doweyko, Lidia
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; et al.
SOURCE: PCT Int. Appl., 265 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009017	A2	20040129	WO 2003-US22300	20030717
WO 2004009017	A3	20040708		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004132758 A1 20040708 US 2003-621909 20030717
PRIORITY APPLN. INFO.: US 2002-396877P P 20020718
OTHER SOURCE(S): MARPAT 140:145835
GI



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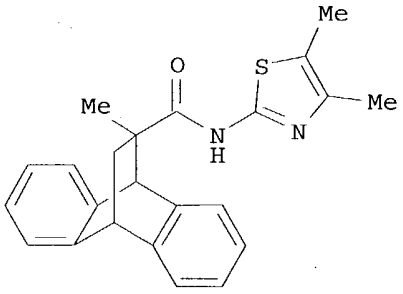


II

AB Title compds. I [R-R4 = H, alk(en/yn)yl, alkoxy, aryl, etc.; Z = carboxamido, alkylamino, etc.] are prepared For instance, 2-amino-4,5-dimethylthiazole is coupled to the acid derived from the cycloaddn. of methacrylic acid and anthracene (CH3CN, EDCI, Et3N, HOAt, 18 h) to give II. I are glucocorticoid receptor modulators which are useful in treating diseases requiring glucocorticoid receptor agonist or antagonist therapy such as obesity, diabetes, inflammatory and immune disorders.

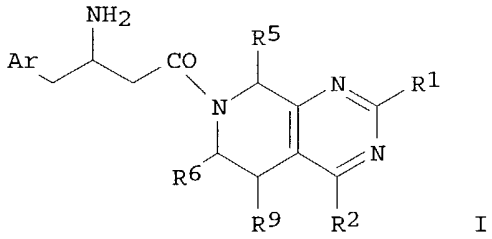
IT **59-67-6**, **Niacin**, biological studies **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid receptor)

L24 ANSWER 23 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:60484 HCAPLUS
DOCUMENT NUMBER: 140:111427
TITLE: Preparation of piperidino pyrimidine dipeptidyl peptidase-IV inhibitors for the treatment of diabetes
INVENTOR(S): Mathvink, Robert J.; Edmondson, Scott D.; Weber, Ann E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007468	A1	20040122	WO 2003-US21758	20030711

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2002-395846P P 20020715
OTHER SOURCE(S): MARPAT 140:111427
GI



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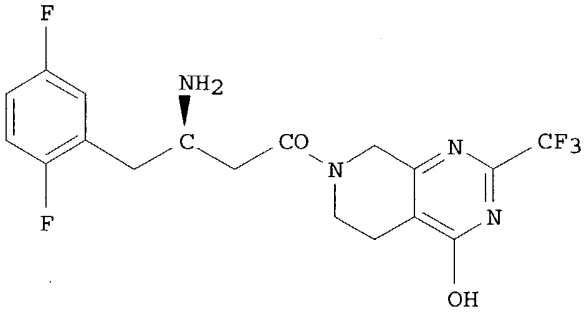


II

AB The present invention is directed to piperidino pyrimidines (shown as I; variables defined below; e.g. II) that are inhibitors of the dipeptidyl peptidase-IV enzyme ('DP-IV inhibitors'; no data) and that are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly Type 2 diabetes. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which the dipeptidyl peptidase-IV enzyme is involved. For I: Ar = Ph (un)substituted with 1-4 R3; R3 = halogen, C1-6alkyl (linear or branched and (un)substituted with 1-5 halogens), OC1-6alkyl (linear or branched and (un)substituted with 1-5 halogens), CN, and OH; R1 and R2 = H, CN, C1-10alkyl (linear or branched and (un)substituted), Ph (un)substituted with 1-5 substituents, a 5- or 6-membered heterocycle which may be (un)saturated comprising 1-4 heteroatoms = N, S and O, the heterocycle being (un)substituted with 1-3 substituents, C3-6cycloalkyl (un)substituted with 1-5 substituents, OH, OR4, and NR7R8; R4 is C1-6alkyl linear or branched and (un)substituted with 1-5 halogen, CO2H, and CO2C1-6alkyl. R5, R6 and R9 = H, C1-10alkyl (linear or branched and (un)substituted with 1-5 substituents), CN, Ph (un)substituted with 1-5 substituents, naphthyl (un)substituted with 1-5 substituents, CO2H, CO2C1-6alkyl, CONR7R8, and C3-6cycloalkyl (un)substituted with 1-5 substituents; R7 and R8 = H, Ph (un)substituted with substituents = halogen, OH, C1-6alkyl, and OC1-6alkyl, C3-6cycloalkyl (un)substituted with substituents = halogen, OH, C1-6alkyl, and OC1-6alkyl, and C1-6alkyl linear or branched and (un)substituted, or wherein R7 and R8 together with the N atom to which they are attached form a heterocyclic ring = azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is (un)substituted with 1-5 halogen, hydroxy, C1-6 alkyl, and C1-6 alkoxy, wherein alkyl and alkoxy are (un)substituted with one to five halogens; addnl. details are given in the claims. Although the methods of preparation are not claimed, example prepns. and/or

characterization data are included for 57 example of I and 13 examples of intermediates. For example, II was prepared in 3 steps starting from trifluoroacetamidine, NaOEt and Et 1-benzyl-3-oxopiperidine-4-carboxylate hydrochloride and involving intermediates 7-(phenylmethyl)-2-(trifluoromethyl)-5,6,7,8-tetrahydropyrido[3,4-d]pyrimidin-4-ol and 2-(trifluoromethyl)-5,6,7,8-tetrahydropyrido[3,4-d]pyrimidin-4-ol acetate.

IT **59-67-6**, Nicotinic acid, biological studies **147098-20-2**, ZD-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of piperidino pyrimidine dipeptidyl peptidase-IV inhibitors for treatment of diabetes)

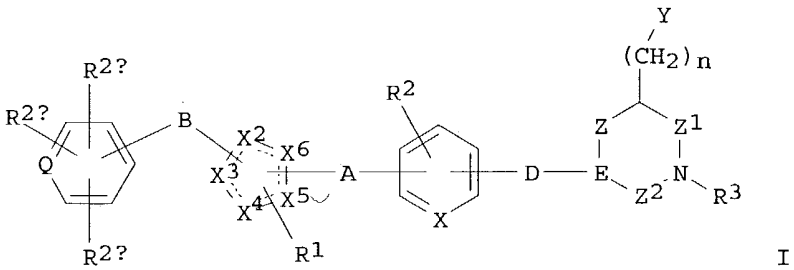
IT **59-67-6D**, Nicotinic acid, salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of piperidino pyrimidine dipeptidyl peptidase-IV inhibitors for treatment of diabetes)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 24 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:41231 HCAPLUS
DOCUMENT NUMBER: 140:111429
TITLE: Preparation of substituted heterocyclic derivatives useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T. W.; Chen, Sean; Devasthale, Pratik; Ding, Charles Z.; Herpin, Timothy F.; Wu, Shung; Zhang, Hao; Wang, Wei; Ye, Xiang-Yang
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 543 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004665	A2	20040115	WO 2003-US22149	20030702
WO 2004004665	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004063700	A1	20040401	US 2003-616365	20030708

PRIORITY APPLN. INFO.: US 2002-394508P P 20020709
OTHER SOURCE(S): MARPAT 140:111429
GI



I

AB The title compds. (I) [Z1 = (CH2)q, CO; Z2 = (CH2)p, CO; D = CH, CO, (CH2)m (where m = 0-3; p = 1, 2; q = 0-2); n = 0-2; Q = C, N; A = (CH2)x (where x = 1-5); A = (CH2)x1 (where x1 = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain; or A = -(CH2)x2-O-(CH2)x3- (where X2, X3 = 0 to 5, provided that at least one of x2 and x3 is other than 0); B = a bond or (CH2)x4 (where x4 = 1-5); X = CH, N; X2-X6 = C, N, O, or S and at least one of X2-X6 is C; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halogen, (un)substituted amino; R2a, R2b, R2c = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, etc.; E = CH, N; Z = (CH2)x5 (where x5 is 0, i.e. a single or a double bond, 1, 2), or Z is (CH2)x6 (where x6 = 2-5), where (CH2)x6 includes an alkenyl (C:C) bond embedded within the chain or Z = -(CH2)x7-O-(CH2)x8- (where x7, x8 = 0-4); (CH2)x to (CH2)x8, (CH2)m, (CH2)n, (CH2)p and (CH2)q may be optionally substituted; Y = CO2R4 (where R4 = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR4a)R5 [where R4a = H, a prodrug ester; R5 = alkyl or aryl, or a phosphonic acid of the structure P(O)(OR4a)2]] including all stereoisomers, prodrug esters, and pharmaceutically acceptable salts thereof are prepared These compds., e.g. cis-1-ethoxycarbonyl-4-[3-[2-(2-phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidin-3-ylacetic acid and cis-1-(6-trifluoromethylpyrimidin-2-yl)-4-[3-[2-(2-phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidine-3-carboxylic acid, modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty acid (NEFA) levels, and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia, hyperinsulinemia, hyperlipidemia, obesity, atherosclerosis, and related diseases employing such substituted acid derivs. alone or in combination with another antidiabetic agent and/or a hypolipidemic agent and/ or other therapeutic agents. Disclosed is a method for treating diabetes, especially Type 2 diabetes, and related diseases such as insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, inflammation, Syndrome X, diabetic complications, dysmetabolic syndrome, atherosclerosis, and related diseases, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I. Also disclosed is a method for treating early malignant lesions (such as ductal carcinoma in situ of the breast and lobular carcinoma in situ of the breast), premalignant lesions including fibroadenoma of the breast and prostatic intraepithelial neoplasia (PIN), liposarcomas and various other epithelial tumors (including breast, prostate, colon, ovarian, gastric and lung), irritable bowel syndrome, Crohn's disease, gastric ulceritis, and osteoporosis and proliferative diseases such as psoriasis, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I.

IT **59-67-6, Niacin**, biological studies **637-07-0, Clofibrate 49562-28-9, Fenofibrate**

287714-41-4, Visastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

L24 ANSWER 25 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:41224 HCAPLUS
DOCUMENT NUMBER: 140:111417
TITLE: Preparation of substituted heterocyclic derivatives useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T. W.; Chen, Sean; Ding, Charles Z.; Herpin, Timothy F.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004655	A2	20040115	WO 2003-US21331	20030708
WO 2004004655	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004063762	A1	20040401	US 2003-616283	20030708
PRIORITY APPLN. INFO.:			US 2002-394553P P	20020709
OTHER SOURCE(S):	MARPAT 140:111417			

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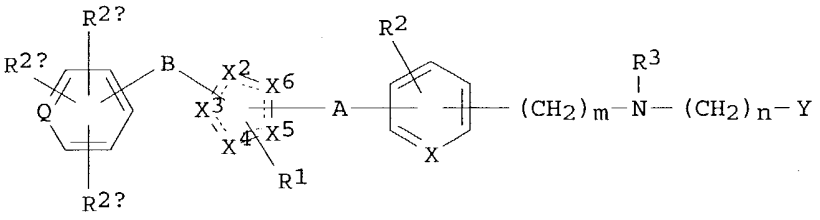


I

AB Compds. having general structure (I) [Q = C, N; A = (un)substituted (CH2)x (where x = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain, or A = (un)substituted -(CH2)x2-O-(CH2)x3- (where x2, x3 = 0-5, provided that at least one of x2 and x3 is other than 0); B = a bond, (un)substituted (CH2)x4 (where x4 = 1-5); X = CH, N; X2-X6= C, N, O, or S, provided that at least one of X2-X6 is N; and at least one of X2, X3, X4, X5 and X6 is C; R1 = H, alkyl; R2, R2a, R2b, R2c = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino,

aryloxycarbonylamino, etc.; Y = CO2R (where R = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR4a)R5 [where R4a = H, a prodrug ester; R5 = alkyl, aryl, or a phosphonic acid of the structure P(O)(OR4a)2]] including all stereoisomers thereof, prodrug esters thereof, and pharmaceutically acceptable salts thereof are prepared These compds. such as N-[[4-(1,2,3-triazol-4-ylmethoxy)benzyl](4-methoxypheoxycarbonyl)amino]acetic acid N-[[4-[2-(1,2,3-triazol-4-yl)ethoxy]benzyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[1-[4-(2- or 4-imidazolylmethoxy)phenyl]isopentyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[1-[4-(1,2,4-oxadiazol-3-ylmethoxy)phenyl]isopentyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[4-(1,2,4-oxadiazol-3-ylmethoxy)phenethyl](isobutoxycarbonyl)amino]acetic acid derivs. modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty acid (NEFA) and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia, hyperinsulinemia, hyperlipidemia, obesity, atherosclerosis, and related diseases.

IT **59-67-6**, **Niacin**, biological studies **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

L24 ANSWER 26 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:10843 HCAPLUS
DOCUMENT NUMBER: 140:399274
TITLE: Metabolism, excretion, and pharmacokinetics of rosuvastatin in healthy adult male volunteers
AUTHOR(S): Martin, Paul D.; Warwick, Mike J.; Dane, Aaron L.; Hill, Steve J.; Giles, Petrina B.; Phillips, Paul J.; Lenz, Eva
CORPORATE SOURCE: AstraZeneca, Macclesfield, UK
SOURCE: Clinical Therapeutics (2003), 25(11), 2822-2835
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Rosuvastatin is a 3-hydroxy-3-methylglutaryl CoA-reductase inhibitor, or statin, that has been developed for the treatment of dyslipidemia. Objective: This study assessed the metabolism, excretion, and pharmacokinetics of a single oral dose of radiolabeled rosuvastatin ([14C]-rosuvastatin) in healthy volunteers. Methods: This was a nonrandomized, open-label, single-day trial. Healthy adult male volunteers were given a single oral dose of [14C]-rosuvastatin 20 mg (20 mL [14C]-rosuvastatin solution, nominally containing 50 μCi radioactivity). Blood, urine, and fecal samples were collected up to 10 days after dosing. Tolerability assessments were made up to 10 days after dosing (trial completion) and at a follow-up visit within 14 days of trial completion. Results: Six white male volunteers aged 36 to 52 yr (mean, 43.7 yr) participated in the trial. The geometric mean peak plasma concentration (Cmax) of rosuvastatin was 6.06 ng/mL and was reached at a median of 5 h after dosing. At Cmax, rosuvastatin accounted for .apprx.50% of the circulating radioactive material. Approx. 90% of the rosuvastatin dose was recovered in feces, with the remainder recovered in urine. The majority of the dose (.apprx.70%) was recovered within 72 h after dosing; excretion was complete by 10 days after dosing. Metabolite profiles in feces indicated that rosuvastatin was excreted largely unchanged (76.8% of the dose). Two metabolites, rosuvastatin-5S-lactone and N-desmethyl rosuvastatin, were present in excreta. [14C]-rosuvastatin was well tolerated; 2 volunteers reported 4 mild adverse events that resolved without treatment. Conclusions: The majority of the rosuvastatin dose was excreted unchanged.

Given the absolute bioavailability (20%) and estimated absorption (.apprx.50%) of rosuvastatin, this finding suggests that metabolism is a minor route of clearance for this agent.

IT **287714-41-4**, Rosuvastatin
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); BIOL (Biological study)
(rosuvastatin metabolism and excretion, and pharmacokinetics in healthy adult male volunteers)

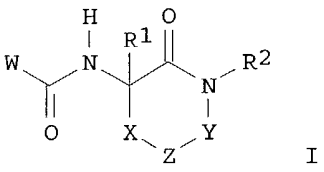
IT **371775-74-5**, N-Desmethyl rosuvastatin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rosuvastatin metabolism and excretion, and pharmacokinetics in healthy adult male volunteers)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 27 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:3661 HCAPLUS
DOCUMENT NUMBER: 140:73181
TITLE: Lactam glycogen phosphorylase inhibitors and their use in disease treatment
INVENTOR(S): Sher, Philip; Wu, Gang; Stouch, Terry; Ellsworth, Bruce
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 51 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004002495	A1	20040101	US 2003-440851		20030519
PRIORITY APPLN. INFO.:			US 2002-382002P	P	20020520

OTHER SOURCE(S): MARPAT 140:73181
GI



I

AB Lactams I (W = bicyclic heteroaryl; X = O, S, SO2, CHR3, CHR3O, CHR3S, CHR3SO2, CHR3CO, CH2CHR3; Y = bond, CHR3; Z = aryl, heteroaryl; R1 = H, alkyl, aryl, alkenyl; R2 = H, alkyl, aryl, arylalkyl, heteroarylalkyl, alkenyl; R3 = H, alkyl, aryl, alkenyl, CN, tetrazole derivative, CO2R4, CONR4R4, CONR4OR4; R4 = H, alkyl, aryl, arylalkyl, heteroarylalkyl, etc.) which are glycogen phosphorylase inhibitors are disclosed. Further provided is a method for treating diabetes and related diseases employing a glycogen phosphorylase inhibiting amount of the above compound, either alone or in combination with another therapeutic agent. Thus, the syntheses of 3-(5-chloroindole-2-carbonylamino)-5-methoxy-3,4-dihydrocarbostyril and 3-(5-chloroindole-2-carbonylamino)-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one, and numerous other related compds., are described.

IT **59-67-6D**, Nicotinic acid, derivs. **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate**
287714-41-4

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactam glycogen phosphorylase inhibitors and)

L24 ANSWER 28 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1007596 HCAPLUS
DOCUMENT NUMBER: 140:65183
TITLE: Oil-containing, orally administrable pharmaceutical composition for improved delivery of a therapeutic agent
INVENTOR(S): Chen, Feng-Jing; Patel, Mahesh V.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Pat. Appl. 2002 32,171.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003235595	A1	20031225	US 2003-397969	20030325
US 6267985	B1	20010731	US 1999-345615	19990630
US 6309663	B1	20011030	US 1999-375636	19990817
US 2001024658	A1	20010927	US 2000-751968	20001229
US 6458383	B2	20021001		
US 2002032171	A1	20020314	US 2001-877541	20010608
US 6761903	B2	20040713		
WO 2004087052	A2	20041014	WO 2004-US9120	20040325

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-345615	A2	19990630
US 1999-375636	A2	19990817
US 2000-751968	A2	20001229
US 2001-877541	A2	20010608
WO 2000-US18807	A	20000710
US 2003-397969	A	20030325

AB The present invention relates to oral pharmaceutical compns. and methods for improved delivery of therapeutic agents, e.g., lipid-regulating agents. Compns. of the present invention include a carrier, where the carrier contains a combination of a triglyceride and at least two surfactants, at least one of which is hydrophilic. Upon dilution with an aqueous medium, the composition forms a clear, aqueous dispersion. The invention also pertains to methods for treating lipid disorders such as hypercholesterolemia, hypertriglyceridemia, and mixed dyslipidemia by oral administration of the compns. provided.

IT **59-67-6**, Nicotinic acid, biological studies **637-07-0**, **Clofibrate 41859-67-0**, **Bezafibrate 49562-28-9**, **Fenofibrate 52214-84-3**, **Ciprofibrate 54504-70-0**, Theofibrate **287714-41-4**, Rosuvastatin
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);

USES (Uses)
(oral composition containing triglyceride and surfactants for improved delivery
of hydrophobic drugs)

L24 ANSWER 29 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:855798 HCAPLUS
DOCUMENT NUMBER: 139:333135
TITLE: Combination therapy including a PPAR α/γ dual agonist, and use in the treatment of hyperglycemia, lipid disorders, and obesity in patients with type 2 diabetes or related disorders
INVENTOR(S): Moller, David E.; Wright, Samuel D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003088962	A1	20031030	WO 2003-US11896	20030415
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2002-373091P	P 20020416
			US 2002-387031P	P 20020607

AB The invention provides pharmaceutical compns. comprising a combination of a first drug which is a PPARα/γ dual agonist and a second drug selected from (1) a cholesterol absorption inhibitor, (2) an HMG-CoA reductase inhibitor, (3) a bile acid sequestrant, (4) nicotinyl alc., nicotinic acid, or a salt thereof, (5) a PPARα agonist, (6) a phenolic antioxidant, (7) an acyl CoA-cholesterol acyltransferase (ACAT) inhibitor, and (8) a cholesterol ester transfer protein (CETP) inhibitor, including pharmaceutically acceptable salts of one or more of the active ingredients, and a pharmaceutically acceptable carrier. Such combinations are useful for treating hyperglycemia, lipid disorders, and obesity in patients who have type 2 diabetes, metabolic syndrome, insulin resistance, and impaired glucose tolerance.

IT **59-67-6**, Nicotinic acid, biological studies **637-07-0**, **Clofibrate 41859-67-0**, **Bezafibrate 49562-28-9**, **Fenofibrate 287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy including PPAR α/γ dual agonist, and use in treatment of hyperglycemia, lipid disorders, and obesity in patients with type 2 diabetes or related disorders)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 30 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:678514 HCAPLUS
DOCUMENT NUMBER: 139:191440

TITLE: Methods of treating or preventing a cardiovascular condition using a cyclooxygenase-1 inhibitor
INVENTOR(S): Krul, Elaine S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003162824	A1	20030828	US 2002-292255		20021112
PRIORITY APPLN. INFO.:			US 2001-331346P	P	20011112
			US 2001-338291P	P	20011113

OTHER SOURCE(S): MARPAT 139:191440

AB Methods for treating or preventing one or more cardiovascular conditions in a subject comprises treating the subject with a therapeutically effective amount of a selective cyclooxygenase-1 inhibitor or a pharmaceutically-acceptable salt, tautomer or prodrug thereof alone or in combination with either a drug used in the treatment or prevention of a cardiovascular condition or a non-drug therapy used in the treatment of a cardiovascular condition. Cyclooxygenase-1 inhibitor, 5-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)pyrazole (I), was prepared from 4'-chloroacetophenone and (4-methoxyphenyl)hydrazine hydrochloride. I inhibited development of atherosclerosis in cholesterol-fed apoE knockout mice.

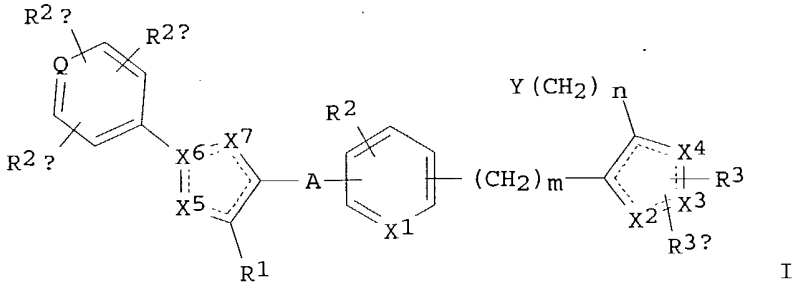
IT **287714-41-4**, Rosuvastatin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid-lowering drug; cyclooxygenase-1 inhibitor for treating or preventing cardiovascular conditions)

IT **437-74-1**, Xanthinolniacinate **6556-11-2**, Inositol niacinate
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peripheral vasodilator; cyclooxygenase-1 inhibitor for treating or preventing cardiovascular conditions)

L24 ANSWER 31 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:656421 HCAPLUS
DOCUMENT NUMBER: 139:197489
TITLE: Preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T.; Zhang, Hao; Hariharan, Narayanan
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 81 pp., Cont.-in-part of U.S. Ser. No. 153,454.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003158232	A1	20030821	US 2002-294525		20021114
US 2003092736	A1	20030515	US 2002-153454		20020522
PRIORITY APPLN. INFO.:			US 2001-294380P	P	20010530
			US 2002-153454	A2	20020522

OTHER SOURCE(S): MARPAT 139:197489
GI



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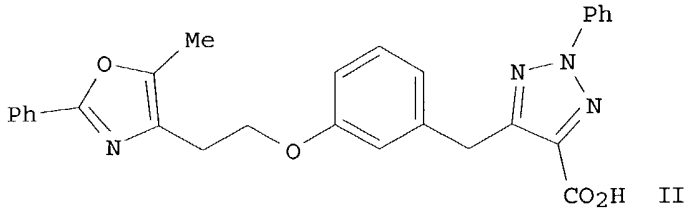


II

AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH2)x, (CH2)x1, (CH2)x2O(CH2)x3; x = 1-5; x1 = 2-5; x2, x3 = 0-5; ≥1 of x2, x3 ≠ 0; X1 = CH, N; X2, X3, X4, X5, X7 = C, N, O, S; in each of X1-X7, C may include CH; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halo, (substituted) amino; R2a, R2b and R2c = H, alkyl, alkoxy, halo, (substituted) amino; R3, R3a = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, etc.; Y = CO2R4, 1-tetrazolyl, P(O)(OR4a)R5, P(O)(OR4a)2; R4 = H, alkyl, prodrug ester; R4a = H, prodrug ester; R5 = alkyl, aryl; with provisos], were prepared as simultaneous inhibitors of peroxisome proliferator activated receptor-γ (PPARγ) and stimulators of peroxisome proliferator activated receptor-α (PPARα). Thus, title compound (II) (prepared starting from Meldrum's acid 3-methoxyphenylacetyl chloride) bound to human PPARα and to PPARγ ligand binding domains with IC50 = 69 nM.

IT **59-67-6**, **Niacin**, biological studies **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**, Visastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

L24 ANSWER 32 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:415607 HCAPLUS
DOCUMENT NUMBER: 140:22930
TITLE: Beneficial effects of rosuvastatin alone and in combination with extended-release **niacin** in patients with a combined hyperlipidemia and low high-density lipoprotein cholesterol levels
AUTHOR(S): Capuzzi, David M.; Morgan, John M.; Weiss, Robert J.; Chitra, Rohini R.; Hutchinson, Howard G.; Cressman, Michael D.
CORPORATE SOURCE: Thomas Jefferson University, Philadelphia, PA, USA
SOURCE: American Journal of Cardiology (2003), 91(11), 1304-1310
CODEN: AJCDAG; ISSN: 0002-9149

PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Patients with combined hyperlipidemia and low high-d. lipoprotein (HDL) cholesterol levels may benefit from combination therapy with a statin and **niacin**; therefore, the authors assessed the efficacy and safety of rosuvastatin and extended-release (ER) **niacin** alone and in combination in 270 patients with this atherogenic dyslipidemia. Men and women ≥18 yr with fasting total cholesterol levels ≥200 mg/dL, triglycerides 200 to 800 mg/dL, apolipoprotein B ≥110 mg/dL, and HDL cholesterol <45 mg/dL were randomized to 1 of 4 treatments in this 24-wk, open-label, multicenter trial: rosuvastatin 10 to 40 mg; ER **niacin** 0.5 to 2 g; rosuvastatin 40 mg/ER **niacin** 0.5 to 1 g; or rosuvastatin 10 mg/ER **niacin** 0.5 to 2 g. Percent changes from baseline in low-d. lipoprotein (LDL) cholesterol, non-HDL cholesterol, and other lipid measurements at week 24 were determined by anal. of variance, with statistical testing performed sep. between the rosuvastatin monotherapy group and each remaining treatment group. Daily doses of rosuvastatin 40 mg reduced LDL and non-HDL cholesterol significantly more than either ER **niacin** 2 g or rosuvastatin 10 mg/ER **niacin** 2 g (-48% vs -0.1% and -36% for LDL cholesterol and -49% vs -11% and -38% for non-HDL cholesterol, resp.; p <0.01 for all comparisons); no addnl. reduction in LDL or non-HDL cholesterol was observed with the combination of rosuvastatin 40 mg/ER **niacin** 1.0 g (-42% and -47%; p = NS). Triglyceride redns. ranged from -21% (ER **niacin** monotherapy) to -39% (rosuvastatin 40 mg/ER **niacin** 1 g), but no observed differences were statistically significant. Compared with rosuvastatin alone, rosuvastatin 10 mg/ER **niacin** 2 g produced significantly greater increases in HDL cholesterol (11% vs. 24%, p <0.001) and apolipoprotein A-I (5% vs. 11%, p <0.017). Similar increases in HDL cholesterol and apolipoprotein A-I were noted between the monotherapy groups. Over 24 wk, rosuvastatin alone was better tolerated than either ER **niacin** alone or the combinations of rosuvastatin and ER **niacin.**
IT **59-67-6**, **Niacin**, biological studies **287714-41-4**, Rosuvastatin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(beneficial effects of rosuvastatin alone and in combination with extended-release **niacin** in humans with combined hyperlipidemia and low high-d. lipoprotein cholesterol levels)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 33 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:376635 HCAPLUS
DOCUMENT NUMBER: 138:362717
TITLE: Combination therapy for treating Alzheimer's disease with HMG-CoA reductase inhibitors and COX-2 inhibitors
INVENTOR(S): MacNeil, Douglas J.; Rosenblum, Charles I.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039542	A1	20030515	WO 2002-US32790	20021011

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-330158P P 20011017

AB The instant invention provides a drug combination comprised of an HMG-CoA reductase inhibitor in combination with a COX-2 inhibitor, which is useful for treating or preventing Alzheimer's disease.

IT **59-67-6**, **Niacin**, biological studies **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Alzheimer's disease treatment with combination of HMG-CoA reductase and COX-2 inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 34 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:320036 HCAPLUS
DOCUMENT NUMBER: 138:338498
TITLE: Preparation of human glucagon-like-peptide-1 mimics and their use in the treatment of diabetes and related conditions
INVENTOR(S): Natarajan, Sesha I.; Bastos, Margarita M.; Bernatowicz, Michael S.; Mapelli, Claudio; Lee, Ving; Ewing, William R.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033671	A2	20030424	WO 2002-US33386	20021018

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-342015P P 20011018
OTHER SOURCE(S): MARPAT 138:338498

AB The invention provides novel human glucagon-like peptide-1 (GLP-1) peptide mimics A-Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa8-Xaa9-Y-Z-B [Xaa1-Xaa9 are naturally or non-naturally occurring amino acid residues; Y and Z are amino acid residues which may be substituted; A and B are optionally present; A is H, an amino acid or peptide containing .apprx. 1-15 amino acid residues, an R group [H, (cyclo)alkyl, cycloalkylalkyl, heterocyclyl, heterocycloalkyl, (hetero)aryl, arylalkyl, aryloxyalkyl, heteroarylalkyl, or heteroaryloxyalkyl], an RCO (amide) group, a carbamate group, a urea, a

sulfonamido, or an aminosulfonyl group; B is OH, alkoxy, etc., an amino or amino acid residue, or a peptide containing from 1-15 amino acid residues, terminating at the C-terminus as a carboxamide, ester, carboxyl, or an amino alc.] that mimic the biol. activity of the native GLP-1 peptide and thus are useful for the treatment or prevention of diseases or disorders associated with GLP activity. These chemical-modified peptides stimulate insulin secretion in type II diabetics and produce other beneficial insulinotropic responses, while exhibiting increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral administration. A method of preparing the polypeptides comprises replacing the message sequence of the polypeptide with a variant message sequence capable of inducing receptor mediated signal transduction. An example is claimed peptide H-AEGTFTSD-Bip(2-Et)-Bip(2-Me)-NH2 (Bip = biphenylalanine residue).

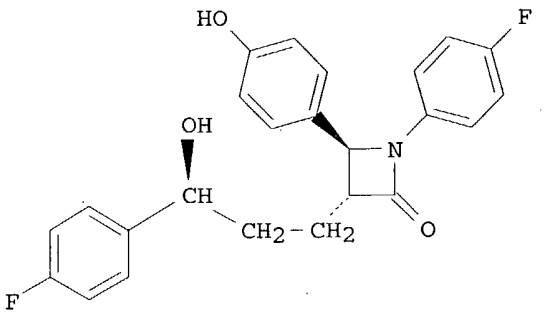
IT **637-07-0, Clofibrate 49562-28-9, Fenofibrate 287714-41-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

L24 ANSWER 35 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:261662 HCAPLUS
DOCUMENT NUMBER: 138:265700
TITLE: Methods and therapeutic combinations for the treatment of xanthoma using sterol/5α-stanol absorption inhibitors
INVENTOR(S): Davis, Harry R.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026643	A2	20030403	WO 2002-US29652	20020919
WO 2003026643	A3	20030703		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003119809	A1	20030626	US 2002-247095	20020919
EP 1429756	A2	20040623	EP 2002-773469	20020919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-323942P P 20010921
WO 2002-US29652 W 20020919

OTHER SOURCE(S): MARPAT 138:265700
GI



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AB The invention provides therapeutic combinations and methods including at least one sterol or 5α-stanol absorption inhibitor that can be useful for treating xanthomas. Compds. of the invention include azetidinone derivative I (preparation described).

IT **59-67-6**, Nicotinic acid, biological studies **59-67-6D**, Nicotinic acid, derivs. **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sterol/5α-stanol absorption inhibitors for treatment of xanthoma, and use with other agents)

L24 ANSWER 36 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:261607 HCAPLUS
DOCUMENT NUMBER: 138:265599
TITLE: Screening and selection methods for statin drug combinations
INVENTOR(S): Prueksaritanont, Thomayant
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003026573	A2	20030403	WO 2002-US30004		20020920
WO 2003026573	A3	20040812			
W: CA, JP, US					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR					
EP 1465667	A2	20041013	EP 2002-763681		20020920
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK					
US 2004180392	A1	20040916	US 2004-490462		20040323
PRIORITY APPLN. INFO.:			US 2001-324485P	P	20010924
			US 2002-378612P	P	20020507
			WO 2002-US30004	W	20020920

AB A method for screening statins in their open acid form to determine the susceptibility of each tested statin to metabolic glucuronidation is provided. Also provided is a method for determining if a non-statin pharmaceutical drug co-administered with a statin that is susceptible to metabolic glucuronidation in its open acid form, will inhibit the glucuronidation of the statin and thereby increase the risk of an adverse drug interaction.

IT **503610-44-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)

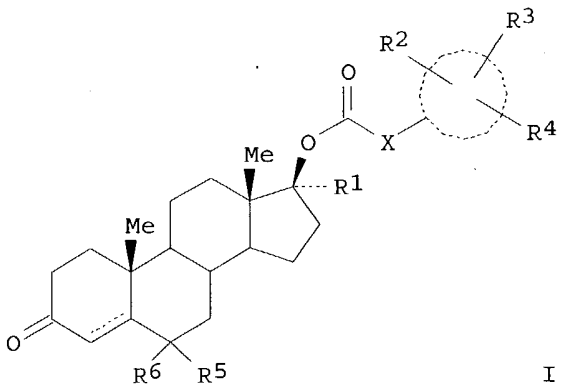
(screening and selection methods for statin drug combinations)

IT **49562-28-9, Fenofibrate 287714-41-4,** Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(screening and selection methods for statin drug combinations)

L24 ANSWER 37 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:261603 HCAPLUS
DOCUMENT NUMBER: 138:281598
TITLE: Androstane compounds as androgen receptor (AR) modulators for the treatment of AR-related diseases
INVENTOR(S): Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026568	A2	20030403	WO 2002-US29436	20020917
WO 2003026568	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1429779	A2	20040623	EP 2002-766288	20020917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004235808	A1	20041125	US 2004-489072	20040308
PRIORITY APPLN. INFO.:			US 2001-324124P	P 20010921
			WO 2002-US29436	W 20020917

OTHER SOURCE(S): MARPAT 138:281598
GI



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AB Compds. of structural formula (I) as herein defined are claimed as useful in a method for modulating a function of the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of activating the function of the androgen receptor in a patient, and in particular the method wherein the function of the androgen receptor is blocked in the prostate of a male patient or in the uterus of a female patient and activated in bone and/or muscle tissue. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteopenia, osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, female sexual dysfunction, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, prostate cancer, inflammatory arthritis and joint repair, alone or in combination with other active agents. Methods for the co-administration of those compds. with bone-strengthening agents are also claimed.

IT **668-56-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(androstane compds. as androgen receptor (AR) modulators for treatment of AR-related diseases)

IT **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androstane compds. as androgen receptor (AR) modulators in conjunction with bone-strengthening agents for treatment of AR-related diseases)

L24 ANSWER 38 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:247122 HCAPLUS
DOCUMENT NUMBER: 139:285675
TITLE: An open-label, randomized, three-way crossover trial of the effects of coadministration of rosuvastatin and **fenofibrate** on the pharmacokinetic properties of rosuvastatin and fenofibric acid in healthy male volunteers
AUTHOR(S): Martin, Paul D.; Dane, Aaron L.; Schneck, Dennis W.; Warwick, Michael J.
CORPORATE SOURCE: AstraZeneca, Cheshire, UK
SOURCE: Clinical Therapeutics (2003), 25(2), 459-471
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Rosuvastatin and **fenofibrate** are lipid-regulating agents with different modes of action. Patients with dyslipidemia who have not achieved treatment targets with monotherapy may benefit from the combination of these agents. The effect of coadministration of rosuvastatin and **fenofibrate** on the steady-state pharmacokinetics of rosuvastatin and fenofibric acid (the active metabolite of **fenofibrate**) was assessed in healthy volunteers. This was an open-label, randomized, 3-way crossover trial consisting of three 7-day treatment periods. Healthy male volunteers received one of the following treatment regimens in each period: rosuvastatin 10 mg orally once daily; **fenofibrate** 67 mg orally TID; and rosuvastatin + **fenofibrate** dosed as above. The steady-state pharmacokinetics of rosuvastatin and fenofibric acid, both as substrate and as interacting drug, were investigated on day 7 of dosing. Treatment effects were assessed by construction of 90% CIs around the ratios of the geometric least-square means for rosuvastatin + **fenofibrate**/rosuvastatin and rosuvastatin + **fenofibrate**/**fenofibrate** for the

area under the plasma concentration-time curve (AUC) and maximum plasma concentration (derived from anal. of variance of log-transformed parameters). Fourteen healthy male volunteers participated in the study. When rosuvastatin was coadministered with **fenofibrate**, there were minor increases in the AUC from 0 to 24 h and maximum concentration (Cmax) of rosuvastatin: the resp. geometric least-square means increased by 7% (90% CI, 1.00-1.15) and 21% (90% CI, 1.14-1.28). The pharmacokinetic parameters of fenofibric acid were similar when **fenofibrate** was dosed alone and with rosuvastatin: the geometric least-square means for fenofibric acid AUC from 0 to 8 h and Cmax decreased by 4% (90% CI, 0.90-1.02) and 9% (90% CI, 0.84-1.00), resp. The treatments were well tolerated alone and in combination. Coadministration of rosuvastatin and **fenofibrate** produced minimal changes in rosuvastatin and fenofibric acid exposure.

IT **49562-28-9**, **Fenofibrate** **287714-41-4**, Rosuvastatin
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rosuvastatin and **fenofibrate** pharmacokinetic interaction in healthy male volunteers)

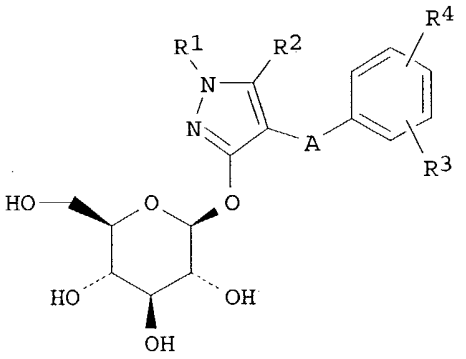
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 39 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:202655 HCAPLUS
DOCUMENT NUMBER: 138:221784
TITLE: Preparation of O-pyrazole glucoside SGLT2 inhibitors as antidiabetic agents
INVENTOR(S): Washburn, William N.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020737	A1	20030313	WO 2002-US28480	20020905
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003087843	A1	20030508	US 2002-235336	20020905
EP 1432720	A1	20040630	EP 2002-761586	20020905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-317280P P 20010905
WO 2002-US28480 W 20020905

OTHER SOURCE(S): MARPAT 138:221784
GI



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AB O-pyrazole glucosides I, wherein A is CH2 or (CH2)2; R1 is hydrogen, arylalkyl, alkenyl, or alkyl; R2 is alkyl or perfluoroalkyl; and R3 and R4 are independently hydrogen, OH, alkoxy, O-aryl, OCH2-aryl, alkyl, cycloalkyl, CF3, -OCHF2, -3,4-(OCH2O), -OCF3, halogen, -CN, carboxylate, -CO2H, acyl, amide, sulfonamide, Aryl, sulfide, sulfoxide; R3 and R4 together with the carbons to which they are attached form an annulated five, six or seven membered carbocycle or heterocycle which may contain 1 to 4 heteroatoms in the ring which are N, O, S, SO, SO2. Further provided are methods of using such compds. for the treatment of diabetes and related diseases, and to pharmaceutical compns. containing such compds. Thus I (A = CH2; R1 = R3 = R4 = H; R2 = Me) was prepared as antidiabetic, anti-obesity, anti-hypertensive, anti-atherosclerotic, and lipid-lowering agent.

IT **637-07-0, Clofibrate 49562-28-9, Fenofibrate 287714-41-4**, Visastatin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of O-pyrazole glucoside SGLT2 inhibitors as antidiabetic agents)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 40 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:154239 HCAPLUS
DOCUMENT NUMBER: 138:180718
TITLE: Combination of a soluble guanylate cyclase stimulant and hypolipemic agent for the treatment of coronary heart disease and other diseases
INVENTOR(S): Bischoff, Hilmar; Stasch, Johannes-Peter
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015770	A1	20030227	WO 2002-EP8701	20020805

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10140421	A1	20030306	DE 2001-10140421		20010817
EP 1429760	A1	20040623	EP 2002-794744		20020805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002011954	A	20040921	BR 2002-11954		20020805
US 2004186163	A1	20040923	US 2004-486620		20040210
PRIORITY APPLN. INFO.:			DE 2001-10140421	A	20010817
			WO 2002-EP8701	W	20020805

OTHER SOURCE(S): MARPAT 138:180718

AB The invention relates to a combination preparation that, as pharmaceutically active constituents, contains at least one active ingredient constituent A and at least one active ingredient constituent B, whereby active ingredient constituent A is a direct stimulator of the soluble guanylate cyclase, and active ingredient constituent B is a lipid reducer. Both active ingredient constituents A and B can be used either simultaneously or in a temporally graduated manner, i.e. exist as a functional unit or sep. from one another.

IT **59-67-6**, Nicotinic acid, biological studies **59-67-6D**, Nicotinic acid, derivs. **41859-67-0**, **Bezafibrate** **49562-28-9**, **Fenofibrate** **52214-84-3**, **Ciprofibrate** **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of a soluble guanylate cyclase stimulant and hypolipemic agent for treatment of coronary heart disease and other diseases)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 41 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:109641 HCAPLUS
DOCUMENT NUMBER: 138:362008
TITLE: Rosuvastatin: A highly effective new HMG-CoA reductase inhibitor
AUTHOR(S): Olsson, Anders G.; McTaggart, Fergus; Raza, Ali
CORPORATE SOURCE: University Hospital, Linkoping, Swed.
SOURCE: Cardiovascular Drug Reviews (2002), 20(4), 303-328
CODEN: CDREEA; ISSN: 0897-5957
PUBLISHER: Neva Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Rosuvastatin, a new statin, has been shown to possess a number of advantageous pharmacol. properties, including enhanced HMG-CoA reductase binding characteristics, relative hydrophilicity, and selective uptake into/activity in hepatic cells. Cytochrome P 450 (CYP) metabolism of rosuvastatin appears to be minimal and is principally mediated by the 2C9 enzyme, with little involvement of 3A4; this finding is consistent with the absence of clin. significant pharmacokinetic drug-drug interactions between rosuvastatin and other drugs known to inhibit CYP enzymes. Dose-ranging studies in hypercholesterolemic patients demonstrated dose-dependent effects in reducing low-d. lipoprotein cholesterol (LDL-C) (up to 63%), total cholesterol, and apolipoprotein (apo) B across a 1- to 40-mg dose range and a significant 8.4% addnl. reduction in LDL-C, compared with atorvastatin, across the dose ranges of the two agents. Rosuvastatin has also been shown to be highly effective in reducing LDL-C, increasing high-d. lipoprotein cholesterol (HDL-C), and producing favorable modifications of other elements of the atherogenic lipid profile in a wide range of dyslipidemic patients. In patients with mild to moderate hypercholesterolemia, rosuvastatin has been shown to produce large decreases in LDL-C at starting doses, thus reducing the need for

subsequent dose titration, and to allow greater percentages of patients to attain lipid goals, compared with available statins. The substantial LDL-C redns. and improvements in other lipid measures with rosuvastatin treatment should facilitate achievement of lipid goals and reduce the requirement for combination therapy in patients with severe hypercholesterolemia. In addition, rosuvastatin's effects in reducing triglycerides, triglyceride-containing lipoproteins, non-HDL-C, and LDL-C and increasing HDL-C in patients with mixed dyslipidemia or elevated triglycerides should be of considerable value in enabling achievement of LDL-C. And non-HDL-C goals in the numerous patients with combined dyslipidemias or metabolic syndrome who require lipid-lowering therapy. Rosuvastatin is well tolerated alone, and in combination with **fenofibrate**, extended-release **niacin**, and cholestyramine, and has a safety profile similar to that of currently marketed statins. A large, long-term clin. trials program is under way to investigate the effects of rosuvastatin on atherosclerosis and cardiovascular morbidity and mortality.

IT **287714-41-4**, Rosuvastatin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HMG-CoA reductase inhibitor rosuvastatin for treatment of dyslipidemias)

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 42 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:42275 HCAPLUS
DOCUMENT NUMBER: 138:106717
TITLE: Preparation of β-amino tetrahydroimidazo[1,2-a]pyrazines and tetrahydrotrioazolo[4,3-a]pyrazines as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes
INVENTOR(S): Edmondson, Scott D.; Fisher, Michael H.; Kim, Dooseop; MacCoss, Malcolm; Parmee, Emma R.; Weber, Ann E.; Xu, Jinyou
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004498	A1	20030116	WO 2002-US21349	20020705
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003100563	A1	20030529	US 2002-189603	20020705
US 6699871	B2	20040302		
NZ 529833	A	20031219	NZ 2002-529833	20020705
EP 1412357	A1	20040428	EP 2002-749813	20020705
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

BR 2002010866	A	20040629	BR 2002-10866		20020705
JP 2004536115	T2	20041202	JP 2003-510665		20020705
US 2004167133	A1	20040826	US 2003-481353		20031219
PRIORITY APPLN. INFO.:			US 2001-303474P	P	20010706
			WO 2002-US21349	W	20020705

OTHER SOURCE(S): MARPAT 138:106717

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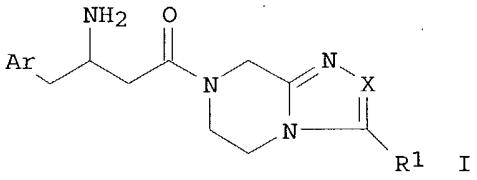

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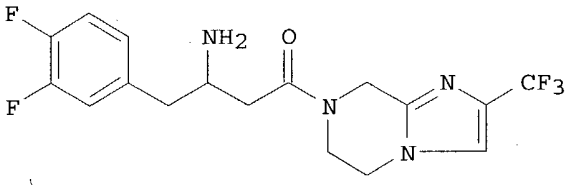

II

AB β-Amino tetrahydroimidazo[1,2-a]pyrazines and tetrahydrotrioazolo[4,3-a]pyrazines [e.g., I; wherein Ar = (substituted) phenyl; X = N, CR2; R1, R2, independently = H, CN, (branched) (substituted) (C1-C10)alkyl, (substituted) Ph, (saturated) 5- or 6-membered heterocycle, etc.] were prepared For example, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)butanoyl]-2-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine (II) was prepared in several steps. The prepared compds. are inhibitors of the dipeptidyl peptidase-IV enzyme ("DP-IV inhibitors") and, thus, are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as type 2 diabetes (no data).

IT **59-67-6**, 3-Pyridinecarboxylic acid, biological studies
147098-20-2, ZD-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination drugs; preparation of β-amino tetrahydroimidazo[1,2-a]pyrazines and tetrahydrotrioazolo[4,3-a]pyrazines as dipeptidyl peptidase inhibitors)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 43 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:20841 HCAPLUS
DOCUMENT NUMBER: 139:190335
TITLE: Management of dyslipidemia in the high-risk patient
AUTHOR(S): Stein, Evan A.
CORPORATE SOURCE: Metabolic and Atherosclerosis Research Center and Medical Research Laboratories International, Cincinnati, OH, USA
SOURCE: American Heart Journal (2002), 144(6, Suppl.), S43-S50
CODEN: AHJOA2; ISSN: 0002-8703
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Lipid-lowering agents have been shown to reduce morbidity and mortality associated with coronary heart disease (CHD), particularly in high-risk patients. The identification and treatment of these patients should therefore be a high priority for clinicians. Guidelines from medical organizations, such as the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) and the American Diabetes Association (ADA), suggest that patients with low-d. lipoprotein cholesterol (LDL-C) levels ≥130 mg/dL, and perhaps even those with levels ≥100 mg/dL, should receive drug therapy. Optimal LDL-C levels have been set at <100 mg/dL and <115 mg/dL for high-risk patients by US and European guidelines, resp. However, a recent survey shows that only about 20% of high-risk patients currently meet these goals. In order to achieve therapeutic targets for LDL-C, the statins are the foundation of treatment, as they are the most effective and best-tolerated form of lipid-lowering therapy. Other therapeutic options include bile acid sequestrants, **niacin**, and plant stanols, although seldom as monotherapy. Combination therapy with a statin and one of these other lipid-lowering agents can be useful in patients who are unable to achieve target lipid levels through monotherapy. There remains, however, a need for addnl. agents. Some of the new options for reducing LDL-C levels that may be available in the near future include 2 new statins, pitavastatin and rosuvastatin. In patients with heterozygous familial hypercholesterolemia, rosuvastatin, which is currently under review by the Food and Drug Administration (FDA), has been shown to produce significantly greater redns. in LDL-C than atorvastatin over its full dose range. In comparative clin. trials, it has also enabled more patients with primary hypercholesterolemia to meet lipid goals than atorvastatin, simvastatin, and pravastatin. Inhibitors of bile acid transport or cholesterol absorption may also have therapeutic value. The first cholesterol absorption inhibitor, ezetimibe, which has just been approved by the FDA, appears to be most effective when combined with a statin. It is anticipated that such new options will allow clinicians to optimize the management of dyslipidemia in high-risk patients, thereby reducing the morbidity and mortality of CHD.

IT **59-67-6**, **Niacin**, biological studies **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(management of dyslipidemia in high-risk patient)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 44 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:5712 HCAPLUS
DOCUMENT NUMBER: 138:73270
TITLE: Preparation of 1-(4-aryl-3-aminobutanoyl)piperazines as dipeptidyl peptidase inhibitors for the treatment of diabetes mellitus
INVENTOR(S): Brockunier, Linda; Parmee, Emma; Weber, Ann E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000181	A2	20030103	WO 2002-US19441	20020619
WO 2003000181	A3	20030227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,

LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1406622 A2 20040414 EP 2002-737543 20020619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2004236102 A1 20041125 US 2003-481359 20031218
PRIORITY APPLN. INFO.: US 2001-299505P P 20010620
WO 2002-US19441 W 20020619
OTHER SOURCE(S): MARPAT 138:73270
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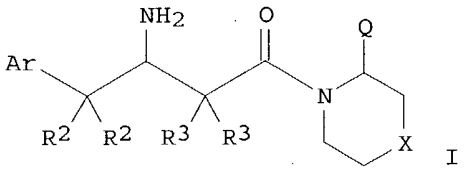

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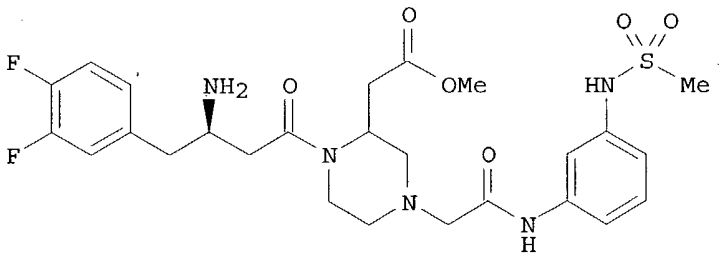


II

AB Title compds. I [wherein X = CH2, O, or NR7; Ar = Ph, naphthyl, thienyl, or benzothiophenyl optionally substituted with 1-5 groups R1; R1 = independently halo, (halo)alkyl, (halo)alkoxy, or CN; R2 = independently H, OH, halo, or (halo)alkyl; or C(R2)2 = (halo)cycloalkyl; R3 = independently H, halo, or (halo)alkyl; or C(R3)2 = (halo)cycloalkyl; Q = H, CN, (un)substituted alkyl, Ph, naphthyl, heterocyclyl, or bicyclyl; C7 = H, (un)substituted (cyclo)alkyl, Ph, heterocyclyl, bicyclyl, adamantyl, or naphthyl; and pharmaceutically acceptable salts and prodrugs thereof] were prepared as inhibitors of the dipeptidyl peptidase-IV enzyme (DP-IV). For example, tert-Bu 2-(2-methoxy-2-oxoethyl)piperazine-1-carboxylate was coupled with α-chloro-3-nitroacetanilide using DIEA in DMF to give the protected piperazine, which was treated with CH2Cl2/TFA to produce Me [4-[2-[(3-nitrophenyl)amino]-2-oxoethyl]piperazin-2-yl]acetate. Amidation with (3R)-3-[(tert-butoxycarbonyl)amino]-4-(3,4-difluorophenyl)butanoic acid, followed by Pd(OH)2 catalyzed hydrogenation, addition of MeSO2Cl, deprotection with CH2Cl2/TFA afforded II•2TFA. Compds. of the invention generally have inhibition consts. of < 10 μM. I and combination therapy including I are useful in the treatment of DP-IV mediated diseases and conditions, such as non-insulin dependent diabetes mellitus (no data).

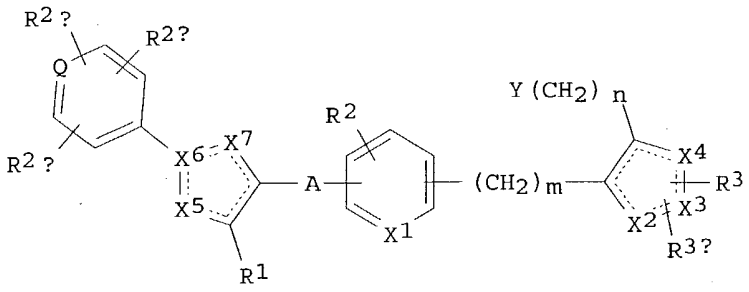
IT **59-67-6**, Nicotinic acid, biological studies **147098-20-2**, ZD-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of [(aryl)(amino)butanoyl]piperazine

dipeptidyl peptidase inhibitors for treatment of diabetes mellitus and related conditions)

L24 ANSWER 45 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:927185 HCAPLUS
DOCUMENT NUMBER: 138:24716
TITLE: Preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T.; Zhang, Hao; Hariharan, Narayanan
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096358	A2	20021205	WO 2002-US16633	20020523
WO 2002096358	A3	20030327		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1390363	A2	20040225	EP 2002-729306	20020523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
TR 200400650	T3	20040621	TR 2004-200400650	20020523
JP 2004536070	T2	20041202	JP 2002-592871	20020523
PRIORITY APPLN. INFO.:			US 2001-294380P	P 20010530
			WO 2002-US16633	W 20020523

OTHER SOURCE(S): MARPAT 138:24716
GI



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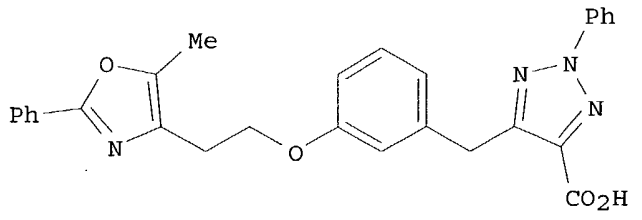

II

AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH2)x, (CH2)x1, (CH2)x2O(CH2)x3; x = 1-5; x1 = 2-5; x2, x3 = 0-5; ≥1 of x2, x3 ≠ 0; X1 = CH, N; X2, X3, X4, X5, X7 = C, N, O, S; in each of X1-X7, C may include CH; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halo, (substituted) amino; R2a, R2b and R2c = H, alkyl, alkoxy, halo, (substituted) amino; R3, R3a = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, alkyl(halo)aryloxycarbonyl, alkoxy(halo)aryloxycarbonyl, cycloalkylaryloxycarbonyl, cycloalkyloxyaryloxycarbonyl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroarylheteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkyl, aminocarbonyl, substituted aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aryloxyarylalkyl, alkynyloxycarbonyl, haloalkoxyaryloxycarbonyl, alkoxycarbonylaryloxycarbonyl, aryloxyaryloxycarbonyl, arylsulfinylarylcarbonyl, etc.; Y = CO2R4, 1-tetrazolyl, P(O)(OR4a)R5, P(O)(OR4a)2; R4 = H, alkyl, prodrug ester; R4a = H, prodrug ester; R5 = alkyl, aryl; with provisos], were prepared as simultaneous inhibitors of peroxisome proliferator activated receptor-γ (PPARγ) and stimulators of peroxisome proliferator activated receptor-α (PPARα). Thus, title compound (II) (prepared starting from Meldrum's acid 3-methoxyphenylacetyl chloride) bound to human PPARα and to PPARγ ligand binding domains with IC50 = 69 nM.

IT **59-67-6**, **Niacin**, biological studies **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

L24 ANSWER 46 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:927184 HCAPLUS
DOCUMENT NUMBER: 138:14048
TITLE: Preparation of oxazolylethoxyphenylprolines and related compounds as antidiabetic and antiobesity agents.
INVENTOR(S): Cheng, Peter T.; Jeon, Yoon; Wang, Wei
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096357	A2	20021205	WO 2002-US16628	20020523
WO 2002096357	A3	20030925		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,

GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003092697 A1 20030515 US 2002-153342 20020522
EP 1401433 A2 20040331 EP 2002-737192 20020523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 2001-294505P P 20010530
WO 2002-US16628 W 20020523
OTHER SOURCE(S): MARPAT 138:14048
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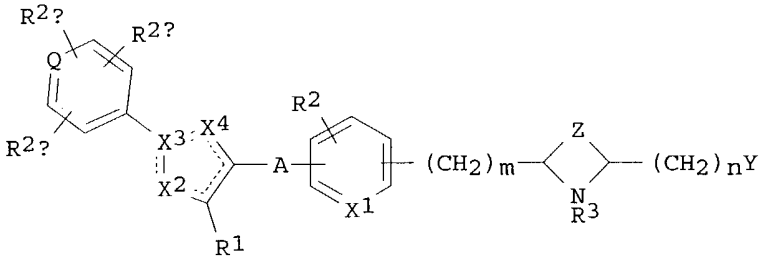

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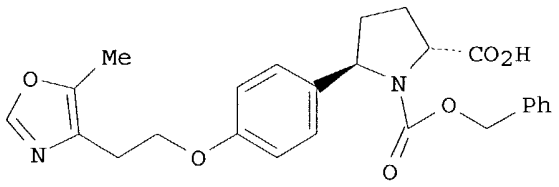


II

AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH2)x, (CH2)x1, with an alkenyl or alkynyl bond in the chain, (CH2)x2O(CH2)x3; x = 1-5; x1 = 2-5; x2, x3 = 0-5; provided that ≥1 of x2 and x3 ≠ 0; X1 = CH, N; X2 = C, N, O, S; X3 = C, N; X4 = C, N, O, S provided that ≥1 of X2, X3, X4 = N; in each of X1-X4, C may include CH; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halo, (substituted) amino; R2a, R2b R2c = H, alkyl, alkoxy, halo, (substituted) amino; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, heteroarylheteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, aryloxyheteroarylalkyl, heteroarylalkyloxyarylalkyl, arylarylalkyl, arylalkenylarylalkyl, arylaminoarylalkyl, etc.; Y = CO2R4, 1-tetrazolyl, P(O)(OR4a)R5, P(O)(OR4a)2; R4 = H, alkyl, prodrug ester; R4a = H, prodrug ester; R5 = alkyl, aryl; Z = (CH2)x4, (CH2)x5, (CH2)x6O(CH2)x7; x4 = 1-5; x5 = 2-5; x6, x7 = 0-4], were prepared as antidiabetic and antiobesity agents (no data). Thus, title compound (II) was prepared in 6 steps.

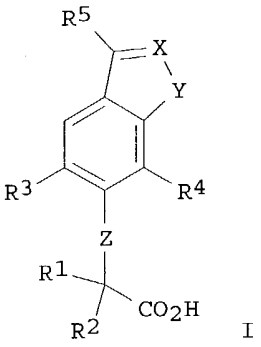
IT **59-67-6**, **Niacin**, biological studies **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of oxazolylethoxyphenylprolines and related compds. as antidiabetic and antiobesity agents)

L24 ANSWER 47 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:889587 HCAPLUS
DOCUMENT NUMBER: 137:370080
TITLE: Preparation of benzisoxazolyloxyacetic acids for treatment of diabetes and lipid disorders
INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 782,856, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002173663	A1	20021121	US 2001-932834	20010817
US 6569879	B2	20030527		
PRIORITY APPLN. INFO.:			US 2000-183593P P	20000218
			US 2001-782856 B2	20010214

OTHER SOURCE(S): MARPAT 137:370080
GI



I

AB Title compds. [I; R1, R2 = H, F, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl; R1R2C = cycloalkyl; R3, R4 = alkyl, alkenyl, alkynyl, Cl; X = N, CR; Y = O, S, NR; Z = O, S; R = H, (substituted) alkyl, alkenyl, alkynyl; R5 = H, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkenyloxy, alkynyloxy, aryl, cycloalkyl, heteroaryl, etc.; with provisos], were prepared as PPARα and/or PPARγ agonists and are therefore useful in the treatment, control or prevention of non-insulin dependent diabetes mellitus, hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, etc. (no data). Thus, 5,7-dipropyl-6-OH-3-CF3-1,2-benzisoxazole (preparation given) was stirred with Me α-bromoisobutyrate and Cs2CO3 in DMF for 7 days at 60° to give Me 2-[(5,7-dipropyl-3-CF3-1,2-benzisoxazol-6-yl)oxy]-2-methylpropionate.

IT **59-67-6**, Nicotinic acid, biological studies **637-07-0**, **Clofibrate 41859-67-0**, Benzafibrate **49562-28-9**, **Fenofibrate 147098-20-2**, Zd-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of benzisoxazolyloxyacetic acids for treatment of diabetes and lipid disorders)

L24 ANSWER 48 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:818798 HCAPLUS
DOCUMENT NUMBER: 138:395431
TITLE: Effects of fibrates on metabolism of statins in human hepatocytes
AUTHOR(S): Prueksaritanont, Thomayant; Tang, Cuyue; Qiu, Yue; Mu,

Lillian; Subramanian, Raju; Lin, Jiunn H.
CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Drug Metabolism and Disposition (2002), 30(11), 1280-1287
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study investigated the metabolic interaction between fibrates and statin hydroxy acids in human hepatocytes. Gemfibrozil (GFZ) modestly affected the formation of β-oxidative products and CYP3A4-mediated oxidative metabolites of simvastatin hydroxy acid (SVA) but markedly inhibited the glucuronidation-mediated lactonization of SVA and the glucuronidation of a β-oxidation product (IC50 .apprx.50 and 15 μM, resp.). In contrast, **fenofibrate** had a minimal effect on all the metabolic pathways of SVA. GFZ also significantly inhibited (IC50 .apprx.50-60 μM) the oxidation of cerivastatin (CVA) and rosuvastatin (RVA), but not of atorvastatin (AVA), while effectively decreasing (IC50 .apprx.30 to 60 μM) the lactonization of all three statins. As was observed previously with other statin hydroxy acids, RVA underwent significant glucuronidation to form an acyl glucuronide conjugate and lactonization to form RVA lactone in human liver microsomes and by UGT 1A1 and 1A3. While GFZ is not an inhibitor of CYP3A4, it is a competitive inhibitor (K1 = 87 μM) of CYP2C8, a major catalyzing enzyme for CVA oxidation These results suggest that (1) the pharmacokinetic interaction observed between GFZ and statins was not likely mediated by the inhibitory effect of GFZ on the β-oxidation, but rather by its effect primarily on the glucuronidation and non-CYP3A-mediated oxidation of statin hydroxy acids, and (2) there is a p.d. between fibrates in their ability to affect the pharmacokinetics of statins, and among statins in their susceptibility to metabolic interactions with GFZ in humans.
IT **49562-28-9**, **Fenofibrate**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of fibrates on metabolism of statins in human hepatocytes)
IT **287714-41-4**, Rosuvastatin
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(effects of fibrates on metabolism of statins in human hepatocytes)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 49 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:813924 HCAPLUS
DOCUMENT NUMBER: 137:311200
TITLE: Preparation of 2,1-oxazoline and 1,2-pyrazoline-based inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Sulsky, Richard B.; Robl, Jeffrey A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

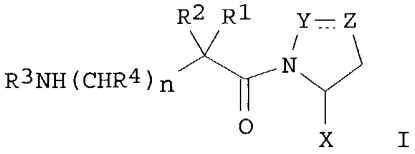
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083128	A1	20021024	WO 2002-US10936	20020405

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002183367	A1	20021205	US 2002-107279		20020326
US 6573287	B2	20030603			
CA 2444465	AA	20021024	CA 2002-2444465		20020405
EP 1377288	A1	20040107	EP 2002-723791		20020405
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004532220	T2	20041021	JP 2002-580932		20020405
PRIORITY APPLN. INFO.:			US 2001-283438P	P	20010412
			WO 2002-US10936	W	20020405

OTHER SOURCE(S): MARPAT 137:311200
GI



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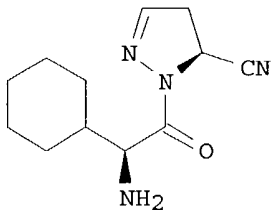


II

AB The invention describes dipeptidyl peptidase IV (DP 4) inhibiting compds. I [n is 0 or 1; X is H or CN; Y is N, NH or O; Z is CH2 when Y is O or NH, with Y-Z forming a single bond, and Z is CH when Y is N, with Y-Z forming a double bond; R1-R4 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl, which may be substituted; R1 may combine with R3 or R4 to form a ring (CR5R6)2-6 or (CR7R8)3-6, resp., where R5-R8 = H, OH, alkoxy, alkyl, aryl, etc.] and their pharmaceutically-acceptable salts or prodrug esters. A method is also provided for treating diabetes and related diseases, employing a DP 4 inhibitor I, optionally in combination with other therapeutic agents, including an antidiabetic, hypolipidemic, or anti-obesity agent. Thus, coupling of sultam-protected 1,2-pyrazoline-3-carboxamide with (S)-N-(tert-butoxycarbonyl)cyclohexylglycine (HOAt, Et3N, and EDAC in CH2Cl2), followed by sultam cleavage with methanolic ammonia, amide conversion to nitrile using imidazole, and deprotection, afforded II.TFA.

IT **637-07-0**, **Clofibrate 49562-28-9**,
Fenofibrate 287714-41-4, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid modulating agent; preparation of oxazoline and pyrazoline-based inhibitors of dipeptidyl peptidase IV)

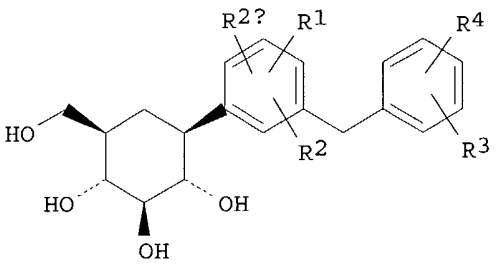
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 50 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:813874 HCAPLUS
DOCUMENT NUMBER: 137:311199
TITLE: Amino acid complexes of C-aryl glucosides for treatment of diabetes
INVENTOR(S): Gougoutas, Jack Z.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083066	A2	20021024	WO 2002-US11066	20020408
WO 2002083066	A3	20030306		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2444481	AA	20021024	CA 2002-2444481	20020408
US 2003064935	A1	20030403	US 2002-117914	20020408
US 6774112	B2	20040810		
EP 1385856	A2	20040204	EP 2002-723801	20020408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004536047	T2	20041202	JP 2002-580871	20020408

PRIORITY APPLN. INFO.: US 2001-283097P P 20010411
WO 2002-US11066 W 20020408

OTHER SOURCE(S): MARPAT 137:311199
GI



I

AB Crystalline complexes are obtained from 1:1 or 2:1 mixts. of either the (D) or (L) enantiomer of natural amino acids and compds. of formula I [R1, R2, R2a = H, OH, OR5, alkyl, OCHF2, OCF3, SR5a, halogen; R3, R4 = H, OH, OR5b, alkyl, cycloalkyl, CF3, OCHF2, OCF3, halogen, CONR6R6a, CO2R5c, CO2H, COR6b, CH(OH)R6c, CH(OR5d)R6d, CN, NHCOR5e, NHSO2R5f, NHSO2-aryl, SR5g, SOR5h, SO2R5i, or a five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms (N, O, S, SO, and/or SO2), or R3 and R4

together with the carbons to which they are attached form an annelated five, six or seven membered carbocycle or heterocycle which may contain 1 to 4 heteroatoms in the ring; R5, R5a-R5i are independently alkyl; R6, R6a-R6d are independently H, alkyl, aryl, alkylaryl or cycloalkyl, or NR6R6a form an annelated five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms in the ring]. A method is also provided for treating diabetes and related diseases employing an SGLT2 (sodium dependent glucose transporters found in the intestine and kidney) inhibiting amount of the above complex alone or in combination with another antidiabetic agent or other therapeutic agent. Thus, I (R1 = 4-Me, R4 = 4-OCHF2, R2, R2a, R3 = H) was prepared by a multistep procedure starting from o-toluic acid, anisole, 2,3,4,6-tetra-O-benzyl-β-D-glucolactone, and CHF2Cl and treated with L-phenylalanine to form the crystalline 1:1 complex.

IT **637-07-0, Clofibrate 49562-28-9, Fenofibrate 287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of amino acid/C-aryl glucoside complexes for treatment of diabetes and related diseases)

L24 ANSWER 51 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:736927 HCAPLUS
DOCUMENT NUMBER: 137:247879
TITLE: Preparation of antidiabetic agents C-aryl glucoside as human SGLT2 inhibitors
INVENTOR(S): Ellsworth, Bruce; Washburn, William N.; Sher, Philip M.; Wu, Gang; Meng, Wei
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. 6,414,126.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002137903	A1	20020926	US 2002-151436	20020520
US 6515117	B2	20030204		
US 6414126	B1	20020702	US 2000-679027	20001004
ZA 2002002604	A	20030703	ZA 2002-2604	20020403
WO 2003099836	A1	20031204	WO 2003-US15591	20030515

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 1999-158773P	P	19991012
US 2000-194615P	P	20000405
US 2000-679027	A2	20001004
US 2002-151436	A	20020520

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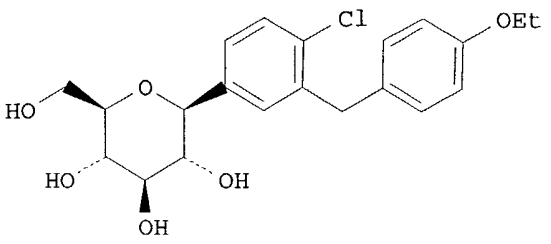

I

AB An SGLT2 inhibiting compound is provided having the formula I method is also provided for treating diabetes and related diseases employing an SGLT2 inhibiting amount of the above compound alone or in combination with another antidiabetic agent or other therapeutic agent (no data). 1A pharmaceutical combination comprising an SGLT2 inhibitor compound and an antidiabetic agent other than an SGLT2 inhibitor, for treating the complications of diabetes, an anti-obesity agent, an antihypertensive agent, an antiplatelet agent, an antiatherosclerotic agent, and/or a lipid-lowering agent (no data). A method for treating or delaying the progression or onset of diabetes, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, delayed wound healing, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis or hypertension, or for increasing high d. lipoprotein levels, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compd (no data).

IT **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**, Rosuvastatin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of antidiabetic agents C-aryl glucosides as human SGLT2 inhibitors)

L24 ANSWER 52 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:637483 HCAPLUS
DOCUMENT NUMBER: 137:185311
TITLE: Preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders
INVENTOR(S): Adams, Alan D.; Jones, A. Brian; Berger, Joel P.; Dropinski, James F.; Elbrecht, Alexander; Liu, Kun; Macnaul, Karen Lamb; Shi, Guo-qiang; Von, Langen Derek J.; Zhou, Gaochao
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064094	A2	20020822	WO 2002-US4680	20020205
WO 2002064094	A3	20030612		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2437118	AA	20020822	CA 2002-2437118		20020205
EP 1366012	A2	20031203	EP 2002-721022		20020205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004521124	T2	20040715	JP 2002-563891		20020205
US 2004092596	A1	20040513	US 2003-470954		20030730
PRIORITY APPLN. INFO.:			US 2001-267809P	P	20010209
			WO 2002-US4680	W	20020205

OTHER SOURCE(S): MARPAT 137:185311

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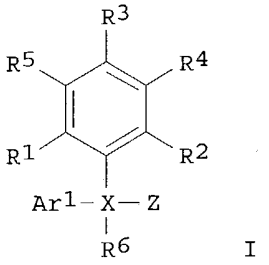

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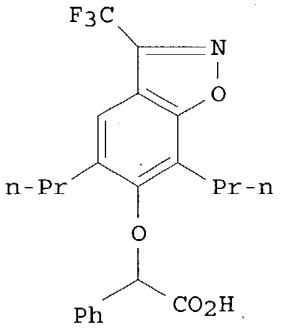

II

AB Title compds. I [R1 = halo, alkyl, alkoxy; R2 = alkyl, alicyclic; R3 = alkyl, aryl, alicyclic, heterocycle, etc.; R4 = H, OH, alkoxy, aryloxy, halo or R3-4 may be joined together to yield 5- or 6-membered heterocycle; R5 = H, halo; R6 = H, halo, CH3, CF3; Ar1 = Ph, thienyl, thiazolyl, oxazolyl, pyridyl; X = O, S; Z = COOH, tetrazole, carboxamide] were prepared For instance, 2,4-dipropylresorcinol was converted to 2,4-dihydroxy-3,5-dipropyl-α,α,α-trifluoroacetophenone (CH2Cl2, TFAA, AlCl3) and subsequently treated with i. hydroxylamine•HCl, MeOH, reflux; ii. Ac2O; iii. pyridine, reflux which afforded 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. The benzisoxazole was reacted with Me 2-bromo-2-phenylacetate (DMF, Cs2CO3) and the product saponified to give II. I are potent agonists of the peroxisome proliferator activated receptor and are useful in the treatment of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR-α and/or PPAR-γ mediated diseases.

IT **59-67-6**, Nicotinic acid, biological studies **637-07-0**, **Clofibrate 41859-67-0**, **Bezafibrate 49562-28-9**, **Fenofibrate 147098-20-2**, ZD-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders)

L24 ANSWER 53 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:594636 HCAPLUS
DOCUMENT NUMBER: 137:135097

TITLE: Acyl sulfamides for treatment of obesity, diabetes and lipid disorders

INVENTOR(S): Jones, A. Brian; Acton, John J., III

PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060388	A2	20020808	WO 2002-US3119	20020125
WO 2002060388	A3	20030227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2434491	AA	20020808	CA 2002-2434491	20020125
EP 1357908	A2	20031105	EP 2002-706128	20020125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004521119	T2	20040715	JP 2002-560584	20020125
US 2004073037	A1	20040415	US 2003-470483	20030729
PRIORITY APPLN. INFO.:			US 2001-264955P P	20010130
			WO 2002-US3119 W	20020125

OTHER SOURCE(S): MARPAT 137:135097

AB A class of acyl sulfamides comprises compds. that are potent ligands for PPARγ receptors and generally have antagonist or partial agonist activity. The compds. may be useful in the treatment, control or prevention of obesity, non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, vascular restenosis, inflammation, and other PPARγ receptor-mediated diseases, disorders and conditions, alone or in combination with one or more other compds. Other compds. are selected from insulin sensitizers, insulin or insulin mimetics, sulfonylureas, α-glucosidase inhibitors, cholesterol lowering agents, PPARδ agonists, antiobesity compds., an ileal bile acid transporter inhibitor, and agents intended for use in inflammatory conditions such as aspirin, nonsteroidal anti-inflammatory drugs, glucocorticoids, azulfidine, and cyclooxygenase-2 selective inhibitors.

IT **59-67-6**, Nicotinic acid, biological studies **637-07-0**, **Clofibrate 41859-67-0**, **Bezafibrate 49562-28-9**, **Fenofibrate 147098-20-2**, ZD-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acyl sulfamides and other drugs for treatment of metabolic disorders mediated by PPARγ receptors)

L24 ANSWER 54 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:575765 HCAPLUS
DOCUMENT NUMBER: 137:140435
TITLE: Benzopyrancarboxylic acid derivatives with PPAR agonist activity for the treatment of diabetes and lipid disorders, and their preparation, pharmaceutical compositions, and use
INVENTOR(S): Sahoo, Soumya P.; Koyama, Hiroo; Miller, Daniel J.; Boueres, Julia K.; Desai, Ranjit C.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103242	A1	20020801	US 2001-21667	20011029
US 6713508	B2	20040330		
CA 2427610	AA	20020808	CA 2001-2427610	20011026
WO 2002060434	A2	20020808	WO 2001-US49501	20011026
WO 2002060434	A3	20030619		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1347755	A2	20031001	EP 2001-997102	20011026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517938	T2	20040617	JP 2002-560626	20011026

PRIORITY APPLN. INFO.: US 2000-244698P P 20001031
WO 2001-US49501 W 20011026

OTHER SOURCE(S): MARPAT 137:140435

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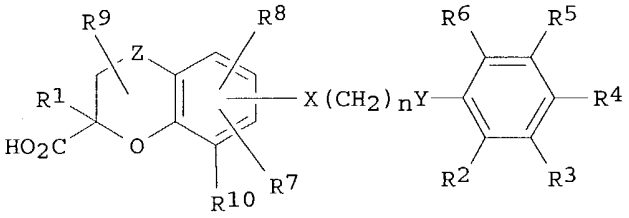

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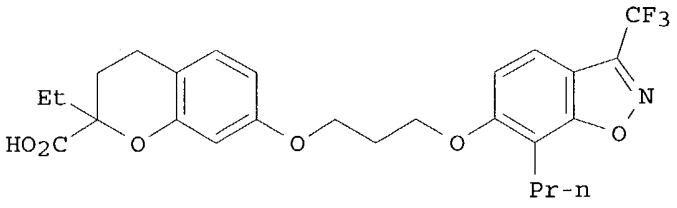

II

AB A class of benzopyrancarboxylic acid derivs. is disclosed, which comprises compds. that are potent agonists (no data) of peroxisome proliferator activated receptors (PPAR) alpha and/or gamma, and are therefore useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR alpha and/or gamma mediated diseases, disorders and conditions. In particular, compds. I and their pharmaceutically acceptable salts and/or prodrugs are disclosed [wherein: Z = CH2, CO; R1 = H, OH, halo, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, or aryl; or R1 forms (un)substituted cyclopropane fusion

to adjacent C atom; X, Y = O, S, SO, SO2, CH2, (un)substituted NH; n = 1-6; R4 = (un)substituted benzoheterocyclyl, cycloalkyl, heterocyclyl, cycloalkyloxy, halo, OH or derivs., alk(en/yn)yl, alk(en/yn)yloxy, or aryl, etc.; other R groups = H, halo, OH, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, aryl, aryloxy, aroyl, etc.; or R3R4 or R4R5 = (un)substituted 5- or 6-membered heterocyclic ring]. A list of 29 compds. is claimed, and their preparation is described. For example, Et 7-hydroxy-4-oxo-4H-chromene-2-carboxylate underwent a sequence of: (1) complete hydrogenation of the enone (98%), (2) etherification of the alc. with PhCH2O(CH2)3Br (66%), (3) alpha ethylation of the ester (70%), (4) hydrogenolytic debenzylation (100%), (5) conversion of the resultant alc. to a bromide (96%), (6) etherification of the bromide with 3-(trifluoromethyl)-7-propyl-6-hydroxybenz[4,5]isoxazole (85%), and (7) alkaline hydrolysis (100%), to give title compound II. PPAR binding assays using human recombinant PPAR are described without data. Co-administration of compds. I with a variety of other drug categories, including a number of specific drugs, is claimed.

IT **59-67-6**, Nicotinic acid, biological studies **59-67-6D**, Nicotinic acid, salts **637-07-0**, **Clofibrate** **41859-67-0**, **Bezafibrate 49562-28-9**, **Fenofibrate 147098-20-2**, ZD-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic compns. also containing; preparation of benzopyrancarboxylic acid derivs. as PPAR agonists for treatment of diabetes and lipid disorders)

L24 ANSWER 55 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2002:574956 HCAPLUS
DOCUMENT NUMBER:	137:129904
TITLE:	Combinations of peroxisome proliferator-activated receptor activators and sterol absorption inhibitors for treatment of vascular diseases
INVENTOR(S):	Kosoglou, Teddy; Davis, Harry R.; Picard, Gilles Jean Bernard
PATENT ASSIGNEE(S):	Schering Corporation, USA
SOURCE:	PCT Int. Appl., 163 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	12

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058732	A2	20020801	WO 2002-US2009	20020125
WO 2002058732	A3	20030703		
WO 2002058732	B1	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2434682	AA	20020801	CA 2002-2434682	20020125
EP 1353696	A2	20031022	EP 2002-714773	20020125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002006654	A	20040225	BR 2002-6654	20020125
EP 1413331	A2	20040428	EP 2004-161	20020125
EP 1413331	A3	20040630		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004521893	T2	20040722	JP 2002-559066		20020125
NO 2003003355	A	20030725	NO 2003-3355		20030725
PRIORITY APPLN. INFO.:			US 2001-264396P	P	20010126
			US 2001-323839P	P	20010921
			EP 2002-714773	A3	20020125
			WO 2002-US2009	W	20020125

OTHER SOURCE(S): MARPAT 137:129904

AB The present invention provides compns., therapeutic combinations and methods including: (a) at least one peroxisome proliferator-activated receptor (PPAR) activator; and (b) at least one substituted azetidinone or substituted β-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols. A tablet contained azetidinone 10, lactose monohydrate 55, microcryst. cellulose 20, povidone 4, croscarmellose sodium 8, sodium lauryl sulfate 2, and magnesium stearate 1 mg. The tablet can be coadministered with a tablets containing a PPAR activator such as ezetimibe. Synthetic preparation of ezetimibe from fluorohenylazetidinone derivs. is described. The coadministration of 10 mg of ezetimibe with 200 mg of **fenofibrate** was well tolerated and caused a significant reduction in LDL-C as compared to either drug alone or placebo.

IT **59-67-6**, Nicotinic acid, biological studies **637-07-0**, **Clofibrate 41859-67-0**, **Bezafibrate 49562-28-9**, **Fenofibrate 52214-84-3**, **Ciprofibrate 287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of peroxisome proliferator-activated receptor activators and sterol absorption inhibitors for treatment of vascular diseases)

L24 ANSWER 56 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2002:540258 HCAPLUS
DOCUMENT NUMBER:	137:109267
TITLE:	Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors
INVENTOR(S):	Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 875,155. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002094977	A1	20020718	US 2001-7407		20011204
US 6627636	B2	20030930			
US 2002013334	A1	20020131	US 2001-875155		20010606
PRIORITY APPLN. INFO.:			US 2000-211595P	P	20000615
			US 2001-875155	A2	20010606

OTHER SOURCE(S): MARPAT 137:109267

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = O, S, SO, SO2, NR7; Z = HOCHCH2CH(OH)CH2CO2R3, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R1, R2 = alkyl, arylalkyl,

cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H, alkyl, metal ion; R4 = H, halo, CF3, etc.; R7 = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R9, R10 = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDl cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). A multistep synthesis of II is reported.

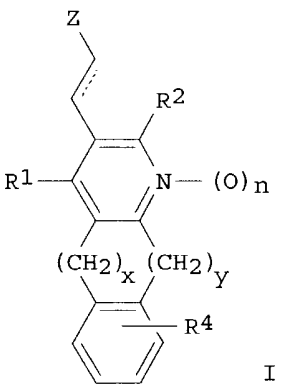
IT **59-67-6**, **Niacin**, biological studies **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

IT **59-67-6D**, Nicotinic acid, derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

L24 ANSWER 57 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:392237 HCAPLUS
DOCUMENT NUMBER: 136:401651
TITLE: Preparation of fused pyridine derivatives as HMG-CoA reductase inhibitors
INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 875,218.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002061901	A1	20020523	US 2001-8154		20011204
US 6620821	B2	20030916			
US 2002028826	A1	20020307	US 2001-875218		20010606
US 2004024216	A1	20040205	US 2003-602753		20030624
PRIORITY APPLN. INFO.:			US 2000-211594P	P	20000615
			US 2001-875218	A2	20010606
			US 2001-8154	A3	20011204

OTHER SOURCE(S): MARPAT 136:401651
GI



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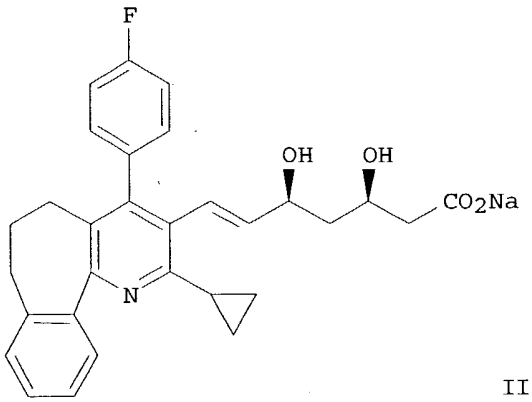


II

AB The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed [wherein: Z = CH(OH)CH2CR7(OH)CH2CO2R3 or corresponding pyranone lactone derivs.; n = 0, 1; x = 0, 1, 2, 3, or 4; y = 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH2)x and/or (CH2)y together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H or lower alkyl; R4 = H, halo, CF3, OH, alkyl, alkoxy, CO2H, (un)substituted NH2, cyano, (un)substituted CONH2, etc.; R7 = H, alkyl]. The compds. are HMG-CoA reductase inhibitors, and are active in inhibiting cholesterol biosynthesis and modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol (no data). I are thus useful in treating hyperlipidemia and dyslipidemia, in hormone replacement therapy, and in treating hypercholesterolemia, hypertriglyceridemia and atherosclerosis, as well as Alzheimer's disease and osteoporosis. Prepns. of several compds. are described. For instance, a multistep synthesis of fused pyridine derivative II is reported. Compds. I may be used in a manner similar to atorvastatin, pravastatin, simvastatin, etc. Combinations of compds. I with various other drugs are claimed, the latter being specified as certain pharmacol. classes, as inhibitors of specific enzymes, as (ant)agonists of specific receptors, and as numerous named drugs.

IT **59-67-6**, Nicotinic acid, biological studies **59-67-6D**, Nicotinic acid, derivs. **637-07-0**, **Clofibrate** **49562-28-9**, **Fenofibrate** **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic compns. also containing; preparation of fused pyridine derivs. as
HMG-CoA reductase inhibitors)

L24 ANSWER 58 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:275818 HCAPLUS
DOCUMENT NUMBER: 136:289065
TITLE: Methods of inhibition of stenosis and/or sclerosis of the aortic valve
INVENTOR(S): O'Brien, Kevin D.; Otto, Catherine M.; Probstfield, Jeffrey L.
PATENT ASSIGNEE(S): University of Washington, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028421	A1	20020411	WO 2001-US31605	20011005
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002011581	A5	20020415	AU 2002-11581	20011005
US 2004057955	A1	20040325	US 2003-398492	20031124
PRIORITY APPLN. INFO.:			US 2000-238367P P	20001006
			WO 2001-US31605 W	20011005

AB The present invention provides methods for decreasing the amount and/or biol. activity of angiotensin II in an aortic valve in an animal. The methods of the invention include administering to the animal an amount of an angiotensin-onverting enzyme antagonist and/or an angiotensin II type 1 receptor antagonist, effective to decrease the amount and/or biol. activity of angiotensin II in the aortic valve in the animal.

IT **59-67-6**, Nicotinic acid, biological studies **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of inhibition of stenosis and/or sclerosis of the aortic valve)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 59 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:240538 HCAPLUS
DOCUMENT NUMBER: 136:268166
TITLE: Spray drying process for preparation of **fenofibrate** compositions
INVENTOR(S): Pace, Gary; Mishra, Awadhesh K.; Snow, Robert A.; Parikh, Indu; Guivarc'h, Pol-Henri
PATENT ASSIGNEE(S): RTP Pharma Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024169	A1	20020328	WO 2001-US12746	20010420
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2423335	AA	20020328	CA 2001-2423335	20010420
AU 2001062945	A5	20020402	AU 2001-62945	20010420
US 2002056206	A1	20020516	US 2001-838593	20010420
US 6696084	B2	20040224		

CA 2440355		AA	20020906	CA 2001-2440355	20010420
WO 2002067901		A1	20020906	WO 2001-US12747	20010420
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002161032		A1	20021031	US 2001-838583	20010420
US 6534088		B2	20030318		
EP 1322289		A1	20030702	EP 2001-937182	20010420
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1361867		A1	20031119	EP 2001-932584	20010420
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004523552		T2	20040805	JP 2002-567269	20010420
US 2004086571		A1	20040506	US 2003-388597	20030317
PRIORITY APPLN. INFO.:				US 2000-234186P	P 20000920
				US 2000-241761P	P 20001020
				US 2001-270157P	P 20010222
				US 2001-838583	A3 20010420
				WO 2001-US12746	W 20010420
				WO 2001-US12747	W 20010420

AB The present invention relates to a novel spray drying process for the preparation of pharmaceutical compns. containing small particles of phospholipid-stabilized **fenofibrate.** This invention also relates to spray dried powdered compns. prepared according to this process and to dosage forms of **fenofibrate** (capsules, tablets, powders, granules, and dispersions) prepared from these powdered compns. The powdered compns. and dosage forms are useful in the treatment of dyslipidemia and dyslipoproteinemia and have the advantage that they provide reduced in vivo variability in the bioavailability of **fenofibrate** active species among fed and fasted patients when administered orally. An admixt. of 3% Lipoid E80 as the surfactant and 10% **fenofibrate** is homogeneously dispersed in pH 8.0 10 mM aqueous phosphate buffer by using a high-shear mixer for 30 min. Mannitol (10%) is then added and the admixt. is heated to 95° during continuous high shear mixing. The heated suspension is then homogenized for 10 batch volume cycles or passes by using a microfluidizer to form a heated homogenate containing the drug. After 10 passes, the heated homogenate is then spray dried to produce a dried powder containing Lipoid E80-stabilized microparticles of **fenofibrate** in mannitol.

IT **49562-28-9**, **Fenofibrate**
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spray drying for preparation of **fenofibrate** compns.)

IT **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spray drying for preparation of **fenofibrate** compns.)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

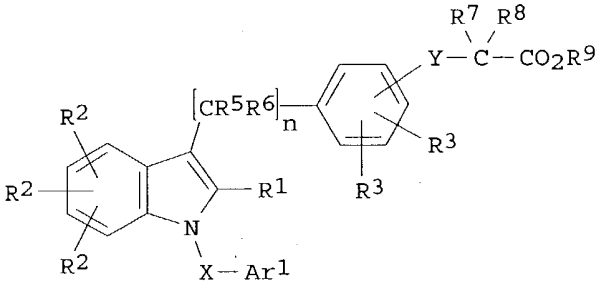
L24 ANSWER 60 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:90008 HCAPLUS
DOCUMENT NUMBER: 136:151071
TITLE: Preparation of N-substituted indoles for treating diabetes
INVENTOR(S): Acton, John J., III; Black, Regina Marie; Jones, Anthony Brian; Wood, Harold Blair

PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008188	A1	20020131	WO 2001-US22979	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2415742	AA	20020131	CA 2001-2415742	20010720
EP 1305285	A1	20030502	EP 2001-954836	20010720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004513076	T2	20040430	JP 2002-514095	20010720
US 2002042441	A1	20020411	US 2001-912961	20010725
US 6525083	B2	20030225		

PRIORITY APPLN. INFO.: US 2000-220778P P 20000725
WO 2001-US22979 W 20010720

OTHER SOURCE(S): MARPAT 136:151071
GI



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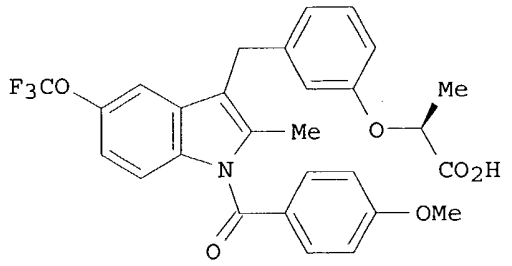


II

AB The title indoles having aryloxyacetic acid substituents [I; R1 = Me, optionally substituted with 1-3 F atoms; R2-R4 = H, halo, alkyl, etc.; R5,

R6 = H, F, OH, alkyl; and R5 and R6 groups that are on the same carbon atom optionally may be joined to form a cyclopropyl group; R7, R8 = H, F, alkyl; or CR7R8 may form cycloalkyl; R9 = H, alkyl; Ar1 = (un)substituted Ph, naphthyl, pyridyl, quinolyl; X = CO, SO2, CH2, CHMe, CMe2, CF2, cyclopropylidene; Y = O, S; n = 0-5] which are agonists or partial agonists of PPAR gamma, and are useful in the treatment, control or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR mediated diseases, disorders and conditions, were prepared E.g., a multi-step synthesis of (2S)-II was given.

IT **59-67-6**, Nicotinic acid, biological studies **637-07-0**, **Clofibrate 49562-28-9**, **Fenofibrate 147098-20-2**, ZD-4522
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-substituted indoles for treating diabetes)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 61 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:833292 HCAPLUS
DOCUMENT NUMBER: 135:344502
TITLE: Preparation of (E)-7-(4-fluorophenyl)-6-isopropyl-2-mesylaminopyrimidin-5-yl)-(3R,5S)-dihydroxyhept-6-enoic acid as HMG-CoA reductase inhibitor
INVENTOR(S): Hill, Steven James; Lenz, Eva Maria; Phillips, Paul John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001085702	A1	20011115	WO 2001-GB1979		20010504
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2404987	AA	20011115	CA 2001-2404987		20010504
EP 1286971	A1	20030305	EP 2001-928070		20010504
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003532715	T2	20031105	JP 2001-582303		20010504
US 2004006097	A1	20040108	US 2002-258065		20021018
PRIORITY APPLN. INFO.:			GB 2000-11163	A	20000510
			WO 2001-GB1979	W	20010504

AB (E)-7[4-(4-fluorophenyl)-6-isopropyl-2-mesylaminopyrimidin-5-yl]-(3R,5S)-dihydroxyhept-6-enoic acid, HMG-CoA reductase inhibitor, was prepared from Me 2-amino-4-(4-fluorophenyl)-6-(1-methylethyl)-5-pyrimidinecarboxylate.

IT **371775-74-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (E)-7-(4-fluorophenyl)-6-isopropyl-2-mesylaminopyrimidin-5-

y)-(3R,5S)-dihydroxyhept-6-enoic acid as HMG-CoA reductase inhibitor)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 62 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:747642 HCAPLUS
DOCUMENT NUMBER: 135:293982
TITLE: Pharmaceuticals containing a β-blocker and a cholesterol-lowering agent
INVENTOR(S): Bondjers, Goeran; Wiklund, Olov; Wikstrand, John
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074394	A1	20011011	WO 2001-SE663	20010327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2403160	AA	20011011	CA 2001-2403160	20010327
EP 1272219	A1	20030108	EP 2001-916044	20010327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001009753	A	20030204	BR 2001-9753	20010327
JP 2003528928	T2	20030930	JP 2001-572136	20010327
EE 200200570	A	20040415	EE 2002-570	20010327
NZ 521351	A	20040827	NZ 2001-521351	20010327
US 2003060477	A1	20030327	US 2002-220790	20020904
ZA 2002007107	A	20031204	ZA 2002-7107	20020904
NO 2002004732	A	20021002	NO 2002-4732	20021002
US 2004192784	A1	20040930	US 2004-824170	20040414

PRIORITY APPLN. INFO.:

SE 2000-1188	A	20000403
SE 2000-2352	A	20000622
WO 2001-SE663	W	20010327
US 2002-220790	B1	20020904

AB The present invention relates to pharmaceutical formulations comprising a β-blocker and a cholesterol-lowering agent in admixt. with an adjuvant, a diluent or carrier, as well as a kit of parts, a method for treatment and use of the formulations for the prophylactic or therapeutic treatment of atherosclerosis, hypercholesterolemia and hyperlipoproteinemia. Thus, a 3-yr placebo-controlled pilot study was designed to investigate the effect of metoprolol succinate controlled-release formulation on atherosclerosis in patients with primary hypercholesterolemia on concomitant therapy with a cholesterol-lowering agent. Total cholesterol, HDL cholesterol and heart rate decreased more in the metoprolol controlled-release group compared with the placebo group.

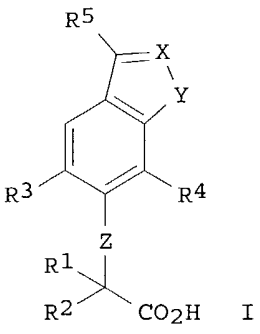
IT **147098-18-8 147098-20-2 287714-41-4**
365453-26-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals containing β-blocker and cholesterol-lowering agent)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 63 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:617987 HCAPLUS
DOCUMENT NUMBER: 135:180757
TITLE: Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of diabetes and lipid disorders
INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian
PATENT ASSIGNEE(S): Merck & Co. Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060807	A1	20010823	WO 2001-US4636	20010214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400021	AA	20010823	CA 2001-2400021	20010214
EP 1259494	A1	20021127	EP 2001-910624	20010214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523336	T2	20030805	JP 2001-560192	20010214
PRIORITY APPLN. INFO.:			US 2000-183593P	P 20000218
			WO 2001-US4636	W 20010214

OTHER SOURCE(S): MARPAT 135:180757
GI



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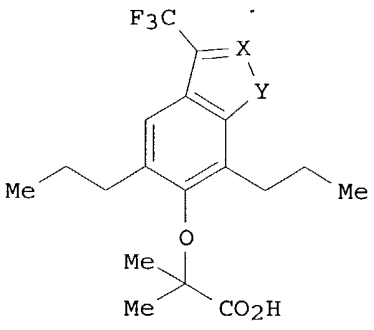


II

AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluoro)alkenyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoro- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or

(un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prepared For example, 2,4-dihydroxy-3,5-dipropyl-1',1',1'-trifluoroacetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. Etherification with Me α-bromoisobutyrate in the presence of Cs2CO3 in DMF, followed by saponification, afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) α and/or γ and are useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPARα and/or γ mediated diseases, disorders, and conditions (no data).

IT **59-67-6**, Nicotinic acid, biological studies **637-07-0**, **Clofibrate 41859-67-0**, **Bezafibrate 49562-28-9**, **Fenofibrate 147098-20-2**, ZD-4522
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration with; preparation of benzisoxazolyloxyacetic acid PPAR agonists via cyclization of dihydroxyacetophenone oximes for treatment of diabetes and lipid disorders)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 64 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:208097 HCAPLUS
DOCUMENT NUMBER: 134:247262
TITLE: Phosphodiesterase inhibitor-hypolipidemic agent combination for the treatment of sexual dysfunction
INVENTOR(S): Bischoff, Erwin; Bischoff, Hilmar; Giuliano, Francois
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019357	A2	20010322	WO 2000-EP8836	20000911
WO 2001019357	A3	20010927		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19944161	A1	20010322	DE 1999-19944161	19990915
CA 2386583	AA	20010322	CA 2000-2386583	20000911
EP 1216039	A2	20020626	EP 2000-965957	20000911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: DE 1999-19944161 A 19990915
WO 2000-EP8836 W 20000911

OTHER SOURCE(S): MARPAT 134:247262

AB A combination preparation is disclosed for the treatment of sexual dysfunction in men or women containing at least one active ingredient A and one active

ingredient B as pharmaceutically active ingredients, in which the active ingredient A is a phosphodiesterase inhibitor, preferably a cGMP phosphodiesterase inhibitor and the active ingredient B a lipid-reducing agent. Both the active ingredients A and B can be administered simultaneously or at alternate intervals, i.e., as a functional unit or separated from each other.

IT **59-67-6**, Nicotinic acid, biological studies **59-67-6D**, Nicotinic acid, analogs **287714-41-4 287714-41-4D**, esters and tautomers
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase inhibitor-hypolipidemic agent combination for the treatment of sexual dysfunction)

L24 ANSWER 65 OF 65 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:553417 HCAPLUS
DOCUMENT NUMBER: 133:144922
TITLE: Drug combinations comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid and an inhibitor, inducer or substrate of P450 isoenzyme 3A4
INVENTOR(S): Raza, Ali; Pears, John Stuart; Hutchinson, Howard Gerard; Schneck, Dennis; Baba, Takahiko; Touchi, Akira; Yamaguchi, Yoshitaka
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Shionogi and Co., Ltd.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000045817	A1	20000810	WO 2000-GB278		20000201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2358632	AA	20000810	CA 2000-2358632		20000201
BR 2000007999	A	20011106	BR 2000-7999		20000201
EP 1185274	A1	20020313	EP 2000-901264		20000201
EP 1185274	B1	20041117			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
TR 200102228	T2	20020321	TR 2001-200102228		20000201
EE 200100406	A	20021015	EE 2001-406		20000201
JP 2002536331	T2	20021029	JP 2000-596937		20000201
NZ 512982	A	20030829	NZ 2000-512982		20000201
AU 767304	B2	20031106	AU 2000-21218		20000201
RU 2233162	C2	20040727	RU 2001-124666		20000201
ZA 2001005838	A	20021016	ZA 2001-5838		20010716
NO 2001003811	A	20011002	NO 2001-3811		20010803
PRIORITY APPLN. INFO.:			GB 1999-2593	A	19990206
			GB 1999-21063	A	19990908
			GB 1999-21064	A	19990908
			WO 2000-GB278	W	20000201

AB The invention concerns safe non-interacting drug combinations of a 3-hydroxy-3-methylglutaryl CoA (HMG-CoA) reductase inhibitor, which is (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid, or a pharmaceutically acceptable salt thereof, (the Agent) and a drug which is either an inducer, inhibitor, or substrate of cytochrome P 450, in particular cytochrome P 450 isoenzyme 3A4. Particular combinations are useful in treating hyperlipidemia in humans who are receiving immunosuppressive chemotherapy. A preferred combination is the Agent and a fibrate drug, the use of such a combination in treating hyperlipidemia in mammals, and medicaments containing such a combination for use in such treatments.

IT **59-67-6, Niacin**, biological studies **637-07-0, Clofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 147098-20-2 287714-41-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dihydroxyheptenoate derivative therapeutic combination)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> => file reg
FILE 'REGISTRY' ENTERED AT 15:13:55 ON 06 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 DEC 2004 HIGHEST RN 792236-36-3
DICTIONARY FILE UPDATES: 5 DEC 2004 HIGHEST RN 792236-36-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

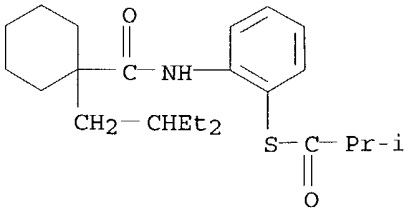
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide can l13 1-36

L13 ANSWER 1 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 791595-08-9 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C23 H35 N O2 S . C22 H28 F N3 O6 S . 1/2 Ca
CI MXS
SR CA
LC STN Files: CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

CM 1

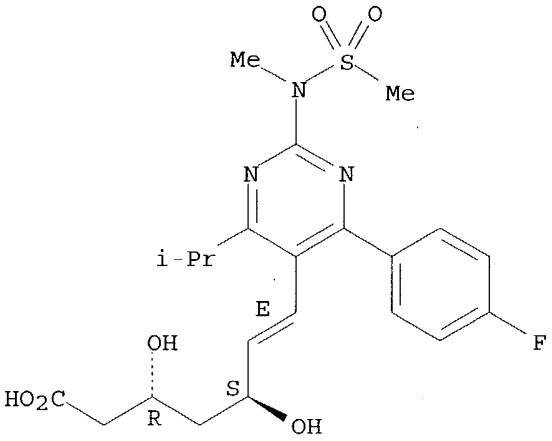
CRN 211513-37-0
CMF C23 H35 N O2 S



CM 2

CRN 147098-20-2 (287714-41-4)
CMF C22 H28 F N3 O6 S . 1/2 Ca

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



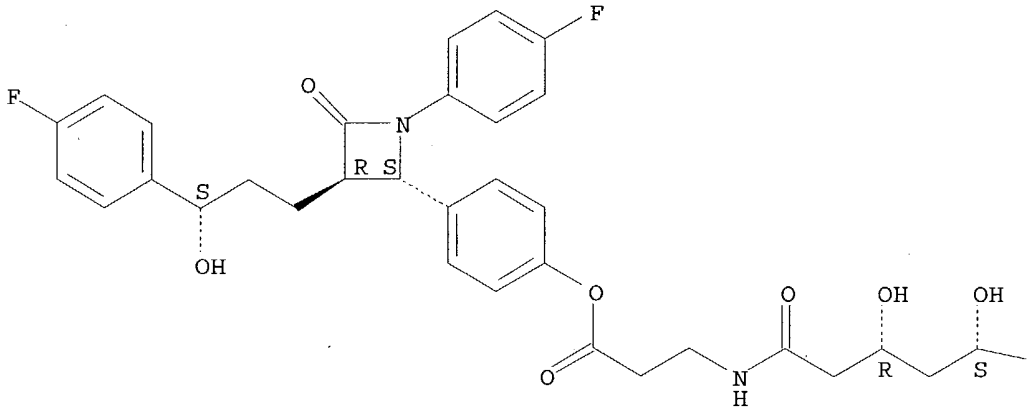
●1/2 Ca

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 2 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 760972-18-7 REGISTRY
CN β-Alanine, N-[(3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-1-oxo-6-heptenyl]-, 4-[(2S,3R)-1-(4-fluorophenyl)-3-[(3S)-3-(4-fluorophenyl)-3-hydroxypropyl]-4-oxo-2-azetidinyl]phenyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C49 H52 F3 N5 O9 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

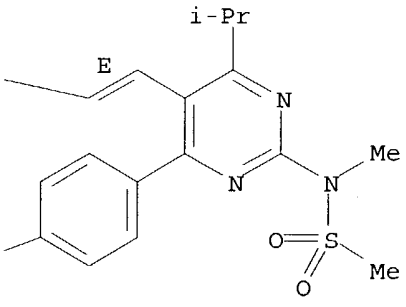
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



F

PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

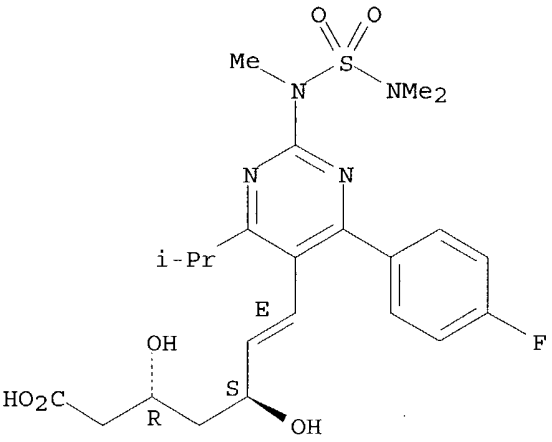
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:277408

L13 ANSWER 3 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 757922-35-3 REGISTRY
CN 6-Heptenoic acid, 7-[2-[[(dimethylamino)sulfonyl]methylamino]-4-(4-fluorophenyl)-6-(1-methylethyl)-5-pyrimidinyl]-3,5-dihydroxy-,

[S-[R*,S*-(E)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H31 F N4 O6 S
CI COM
SR CA

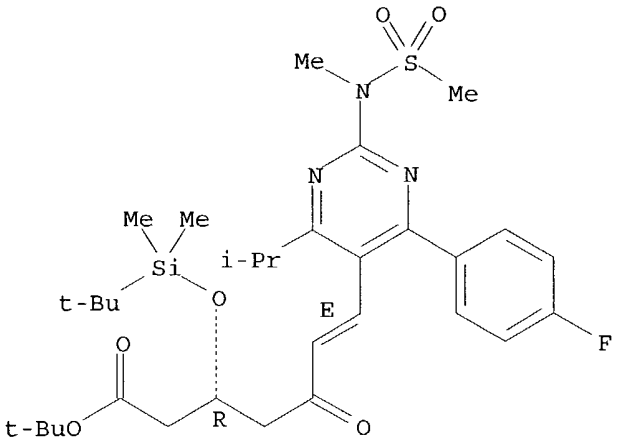
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L13 ANSWER 4 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 676256-39-6 REGISTRY
CN 6-Heptenoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-5-oxo-, 1,1-dimethylethyl ester, (3R,6E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H48 F N3 O6 S Si
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

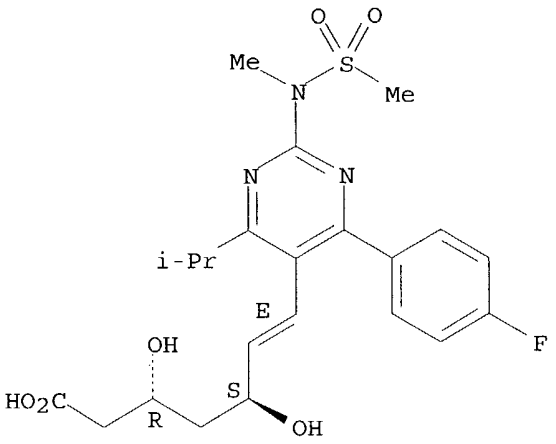
REFERENCE 1: 139:337984

L13 ANSWER 5 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 659737-21-0 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . C4 H11 N O3
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

CM 1

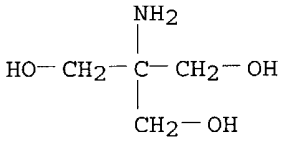
CRN 287714-41-4
CMF C22 H28 F N3 O6 S

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

CRN 77-86-1
CMF C4 H11 N O3

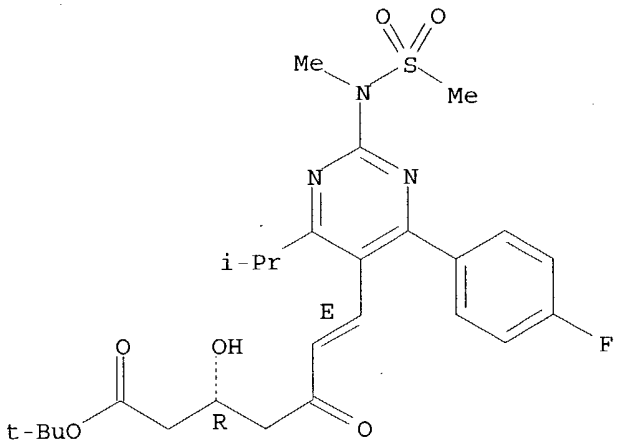


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:187485

L13 ANSWER 6 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615556-96-2 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3-hydroxy-5-oxo-, 1,1-dimethylethyl ester, (3R,6E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H34 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.



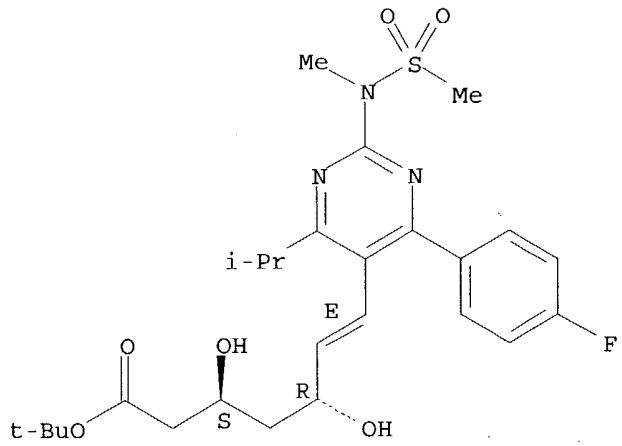
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:337984

L13 ANSWER 7 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615263-60-0 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H36 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)

Relative stereochemistry.
Double bond geometry as shown.



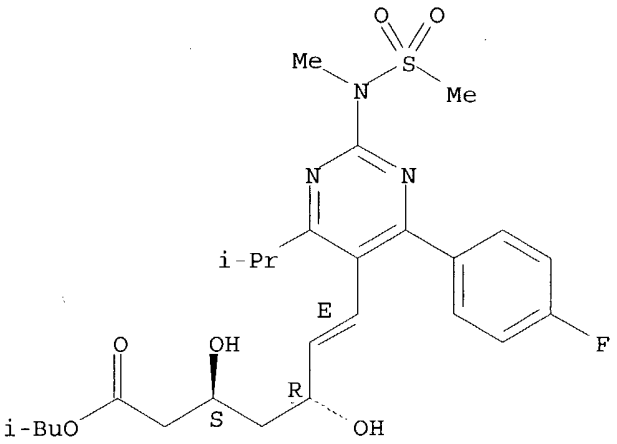
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:323335

L13 ANSWER 8 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615263-59-7 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, 2-methylpropyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H36 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)

Relative stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

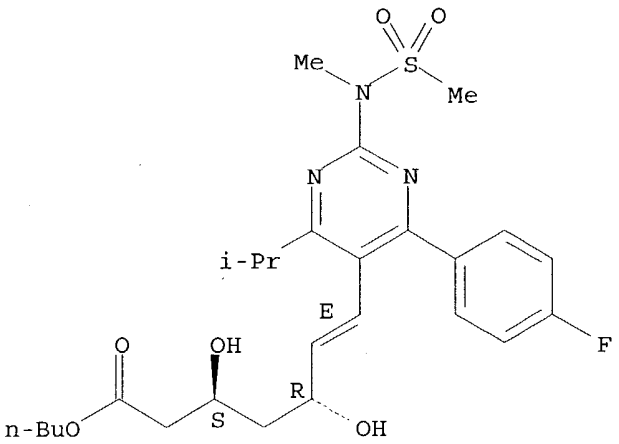
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:323335

L13 ANSWER 9 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615263-58-6 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, butyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H36 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)

Relative stereochemistry.

Double bond geometry as shown.



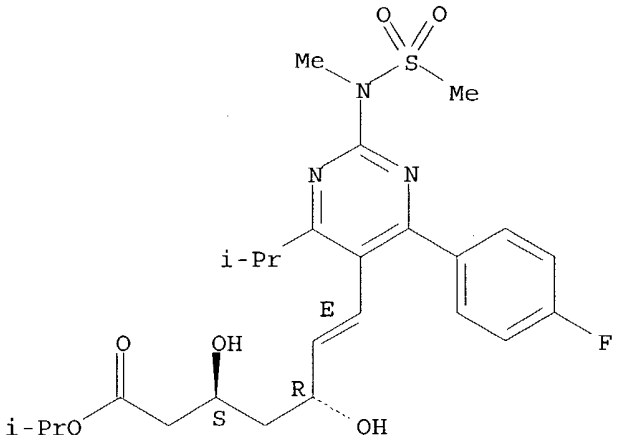
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:323335

L13 ANSWER 10 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615263-57-5 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, 1-methylethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H34 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)

Relative stereochemistry.
Double bond geometry as shown.



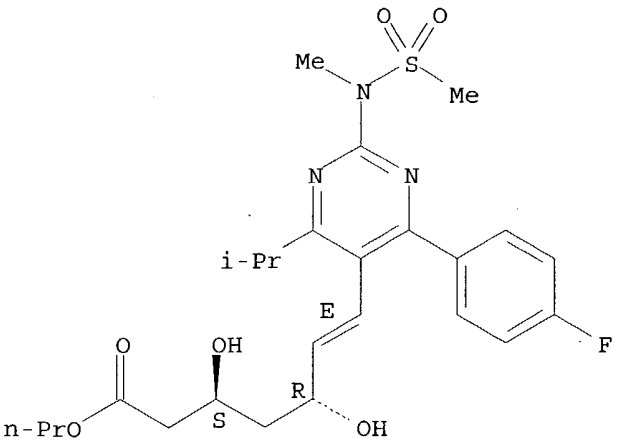
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:323335

L13 ANSWER 11 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615263-56-4 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, propyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H34 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)

Relative stereochemistry.
Double bond geometry as shown.



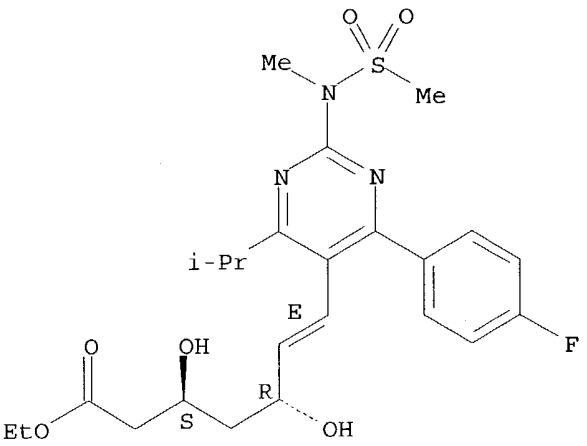
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:323335

L13 ANSWER 12 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615263-55-3 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H32 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)

Relative stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

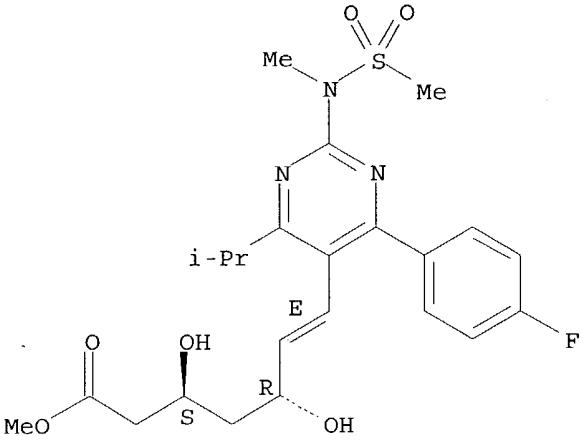
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:323335

L13 ANSWER 13 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615263-54-2 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H30 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)

Relative stereochemistry.

Double bond geometry as shown.



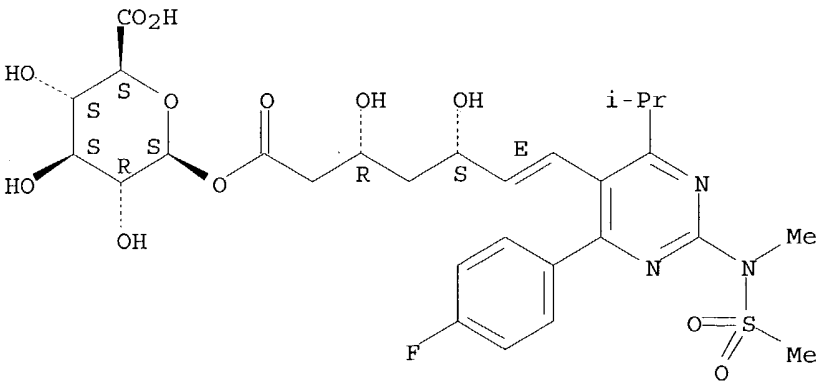
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:323335

L13 ANSWER 14 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 503610-44-4 REGISTRY
CN β-D-Glucopyranuronic acid, 1-[(3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoate] (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H36 F N3 O12 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study)

Absolute stereochemistry.
Double bond geometry as shown.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

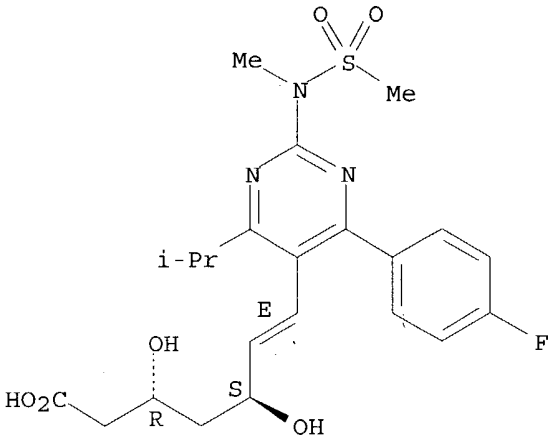
REFERENCE 1: 138:265599

L13 ANSWER 15 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 444313-57-9 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-, mixt. with (3R,4S)-1-(4-fluorophenyl)-3-[(3S)-3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)-2-azetidinone (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H21 F2 N O3 . C22 H28 F N3 O6 S
CI MXS
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

CM 1

CRN 287714-41-4
CMF C22 H28 F N3 O6 S

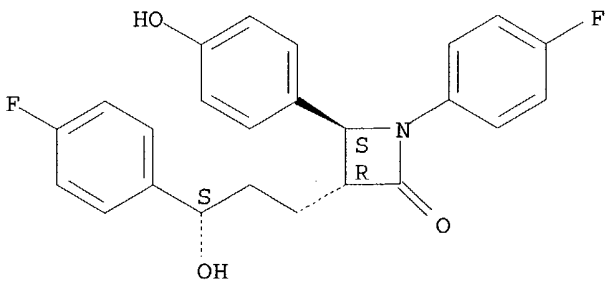
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

CRN 163222-33-1
CMF C24 H21 F2 N O3

Absolute stereochemistry. Rotation (-).

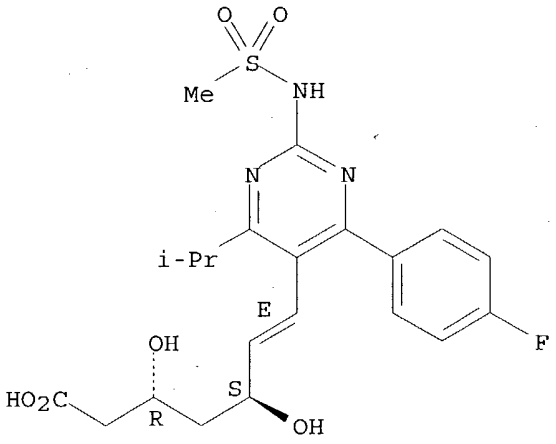


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:135094

L13 ANSWER 16 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 371775-74-5 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN N-Desmethyl rosuvastatin
FS STEREOSEARCH
MF C21 H26 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:388103

REFERENCE 2: 140:417144

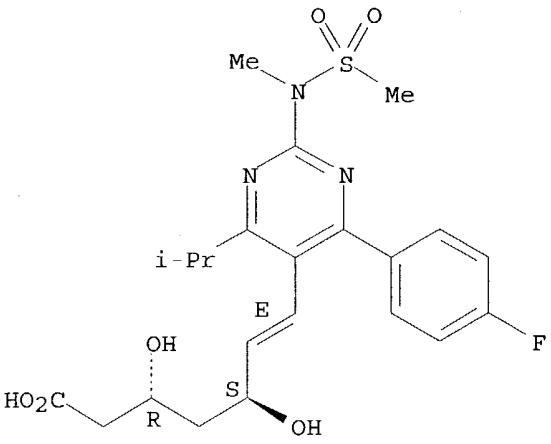
REFERENCE 3: 140:399274

REFERENCE 4: 135:344502

L13 ANSWER 17 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-14-3 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, magnesium

salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . 1/2 Mg
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (287714-41-4)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



●1/2 Mg

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

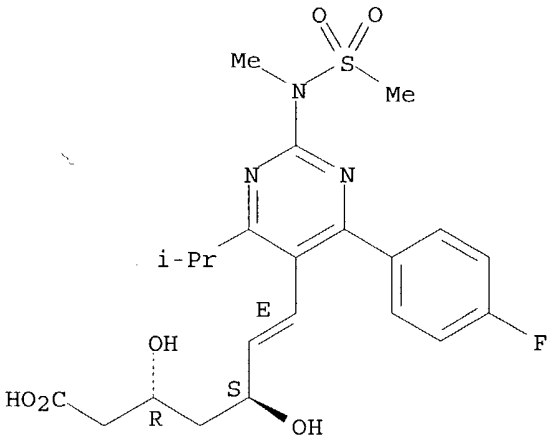
REFERENCE 1: 135:183499

L13 ANSWER 18 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-13-2 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with 4-methoxybenzenemethanamine (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzenemethanamine, 4-methoxy-, (3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoate (9CI)
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . C8 H11 N O
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

CM 1

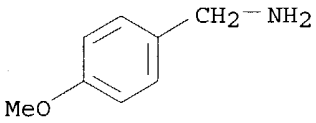
CRN 287714-41-4
CMF C22 H28 F N3 O6 S

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

CRN 2393-23-9
CMF C8 H11 N O



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:183499

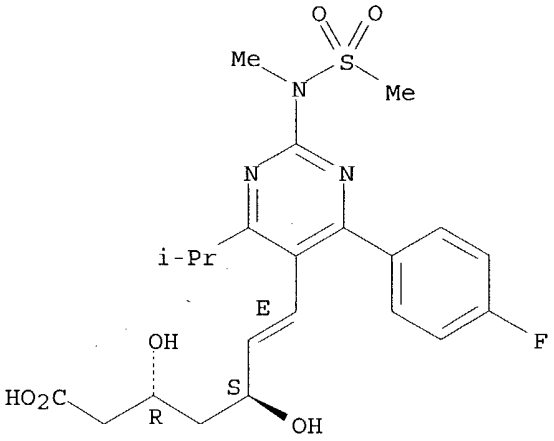
L13 ANSWER 19 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-11-0 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with benzenemethanamine (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzenemethanamine, (3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoate (9CI)
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . C7 H9 N
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

CM 1

CRN 287714-41-4
CMF C22 H28 F N3 O6 S

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



CM 2

CRN 100-46-9
CMF C7 H9 N

H_2N-CH_2-Ph

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

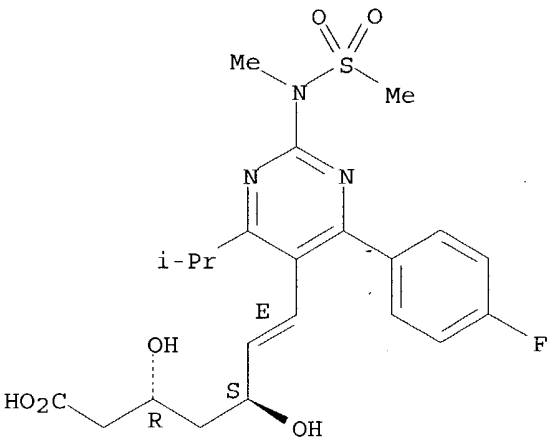
REFERENCE 1: 135:183499

L13 ANSWER 20 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-10-9 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with ethanamine (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethanamine, (3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoate (9CI)
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . C2 H7 N
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

CM 1

CRN 287714-41-4
CMF C22 H28 F N3 O6 S

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

CRN 75-04-7
CMF C2 H7 N

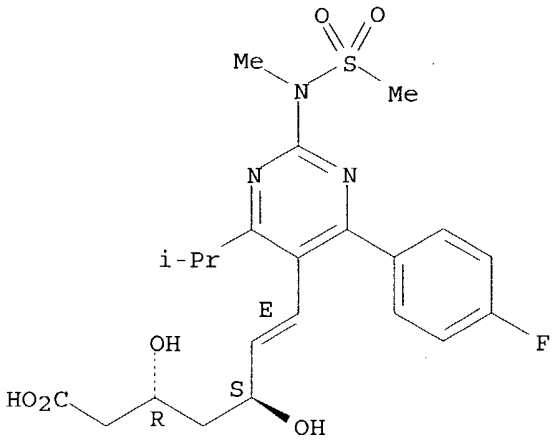
$H_3C-CH_2-NH_2$

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:183499

L13 ANSWER 21 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-08-5 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, monolithium salt, (3R,5S,6E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . Li
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (287714-41-4)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



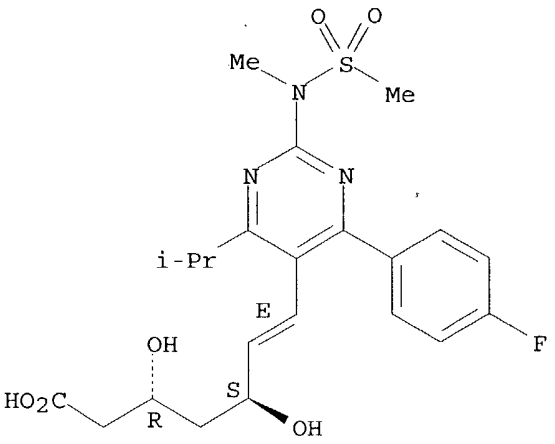
● Li

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:183499

L13 ANSWER 22 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-06-3 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, monoammonium salt, (3R,5S,6E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . H3 N
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
CRN (287714-41-4)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



● NH_3

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:187485

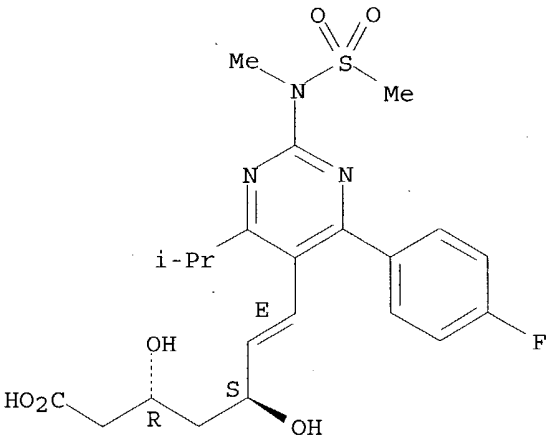
REFERENCE 2: 135:183499

L13 ANSWER 23 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-04-1 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with 2,2'-iminobis[ethanol] (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethanol, 2,2'-iminobis-, (3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoate (salt) (9CI)
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . C4 H11 N O2
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

CM 1

CRN 287714-41-4
CMF C22 H28 F N3 O6 S

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

CRN 111-42-2
CMF C4 H11 N O2

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

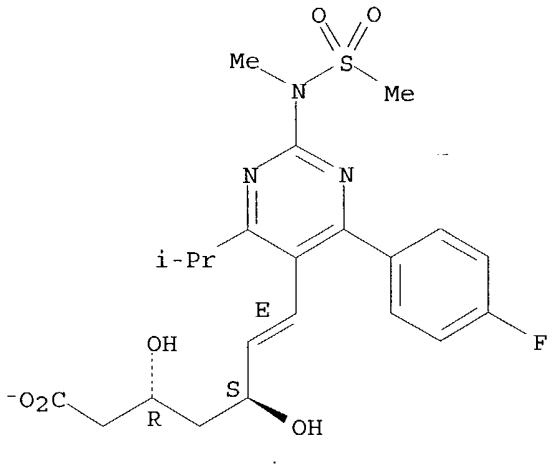
REFERENCE 1: 135:183499

L13 ANSWER 24 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-03-0 REGISTRY
CN Methanaminium, 1-hydroxy-N,N-bis(hydroxymethyl)-N-methyl-, salt with (3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoic acid (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, ion(1-), (3R,5S,6E)-, 1-hydroxy-N,N-bis(hydroxymethyl)-N-methylmethanaminium (9CI)
FS STEREOSEARCH
MF C22 H27 F N3 O6 S . C4 H12 N O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

CM 1

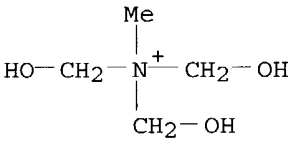
CRN 355806-02-9
CMF C22 H27 F N3 O6 S

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 14433-29-5
CMF C4 H12 N O3

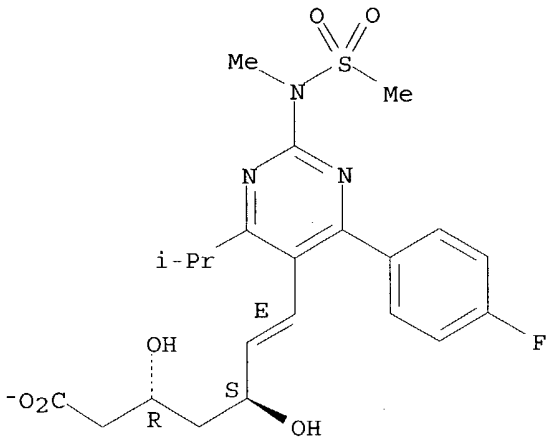


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:183499

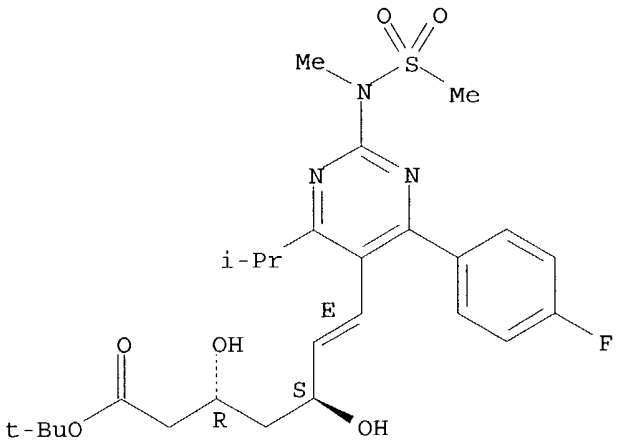
L13 ANSWER 25 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-02-9 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, ion(1-), (3R,5S,6E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H27 F N3 O6 S
CI COM
SR CA

Absolute stereochemistry.
Double bond geometry as shown.



L13 ANSWER 26 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355806-00-7 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H36 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:337984

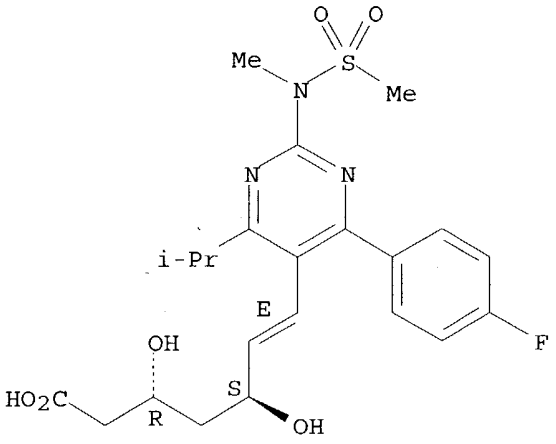
REFERENCE 2: 135:183499

L13 ANSWER 27 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 355805-96-8 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with methanamine (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Methanamine, (3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoate (9CI)
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . C H5 N
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

CM 1

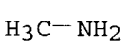
CRN 287714-41-4
CMF C22 H28 F N3 O6 S

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

CRN 74-89-5
CMF C H5 N



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

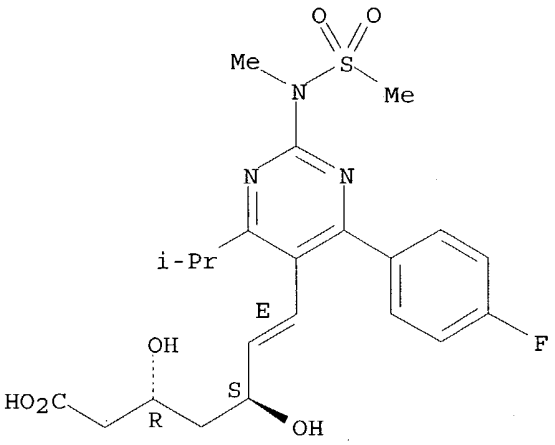
REFERENCE 1: 140:187485

REFERENCE 2: 135:183499

L13 ANSWER 28 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN

RN 287714-41-4 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-(9CI) (CA INDEX NAME)
OTHER NAMES:
CN Rosuvastatin
FS STEREOSEARCH
MF C22 H28 F N3 O6 S
CI COM
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, MEDLINE, MRCK*, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Book; Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

233 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
235 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:395199

REFERENCE 2: 141:388103

REFERENCE 3: 141:384361

REFERENCE 4: 141:374750

REFERENCE 5: 141:374733

REFERENCE 6: 141:343223

REFERENCE 7: 141:343154

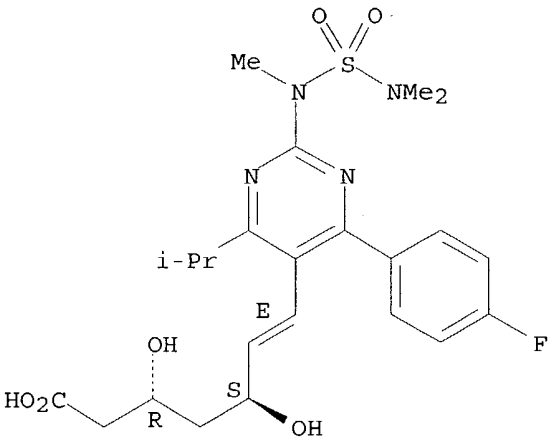
REFERENCE 8: 141:324974

REFERENCE 9: 141:314351

REFERENCE 10: 141:289098

L13 ANSWER 29 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 188557-34-8 REGISTRY
CN 6-Heptenoic acid, 7-[2-[[(dimethylamino)sulfonyl]methylamino]-4-(4-fluorophenyl)-6-(1-methylethyl)-5-pyrimidinyl]-3,5-dihydroxy-, monosodium salt, [S-[R*,S*-(E)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H31 F N4 O6 S . Na
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)
CRN (757922-35-3)

Absolute stereochemistry.
Double bond geometry as shown.



● Na

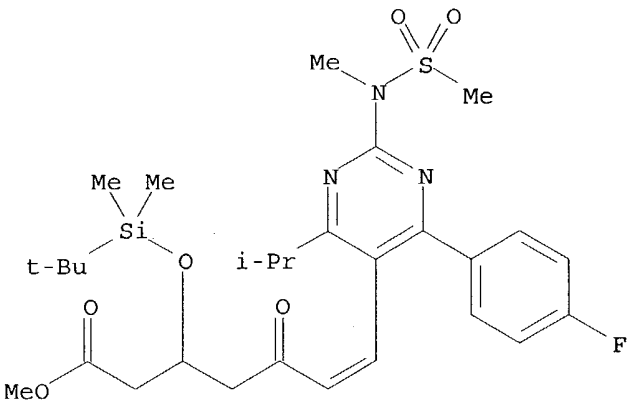
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 126:238350

L13 ANSWER 30 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 169274-76-4 REGISTRY
CN 6-Heptenoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-5-oxo-, methyl ester, (-)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H42 F N3 O6 S Si
SR CA

LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)

Rotation (-).
Double bond geometry unknown.



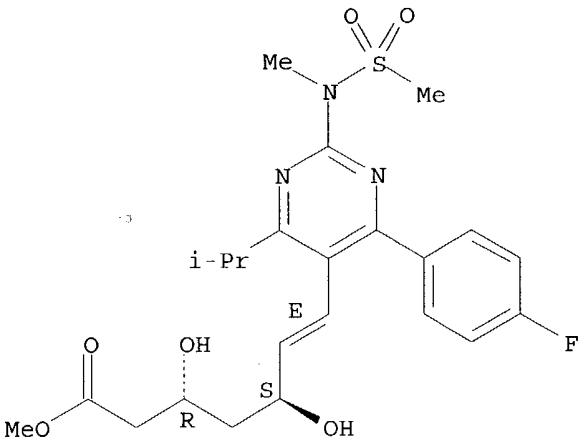
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 123:286068

L13 ANSWER 31 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 147118-40-9 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, methyl ester, [S-[R*,S*-(E)]]-
FS STEREOSEARCH
MF C23 H30 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, PS, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:395947

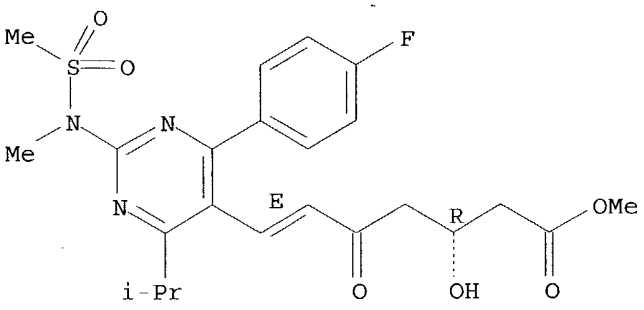
REFERENCE 2: 138:204870

REFERENCE 3: 126:238350

REFERENCE 4: 118:254949

L13 ANSWER 32 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 147118-39-6 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3-hydroxy-5-oxo-, methyl ester, (3R,6E)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3-hydroxy-5-oxo-, methyl ester, [R-(E)]-
FS STEREOSEARCH
MF C23 H28 F N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:54359

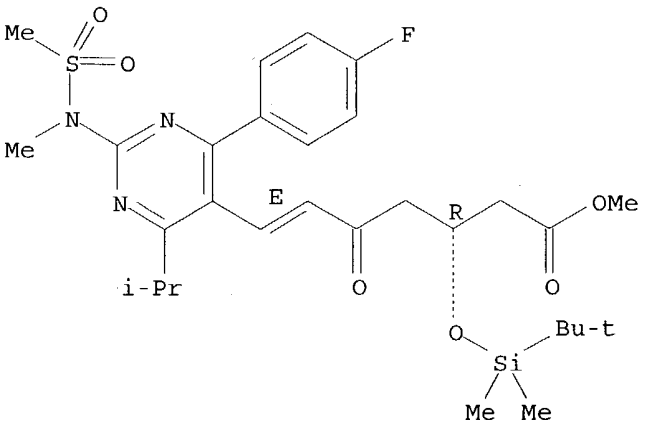
REFERENCE 2: 139:395947

REFERENCE 3: 126:238350

REFERENCE 4: 118:254949

L13 ANSWER 33 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 147118-38-5 REGISTRY
CN 6-Heptenoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-5-oxo-, methyl ester, (3R,6E)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6-Heptenoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-5-oxo-, methyl ester, [R-(E)]-
FS STEREOSEARCH
MF C29 H42 F N3 O6 S Si
SR CA
LC STN Files: CA, CAPLUS, PS, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

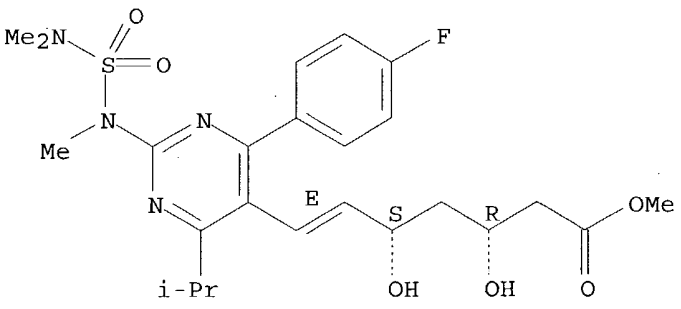
REFERENCE 1: 139:395947

REFERENCE 2: 126:238350

REFERENCE 3: 118:254949

L13 ANSWER 34 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 147118-26-1 REGISTRY
CN 6-Heptenoic acid, 7-[2-[[(dimethylamino)sulfonyl]methylamino]-4-(4-fluorophenyl)-6-(1-methylethyl)-5-pyrimidinyl]-3,5-dihydroxy-, methyl ester, [S-[R*,S*-(E)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H33 F N4 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)

Absolute stereochemistry.
Double bond geometry as shown.



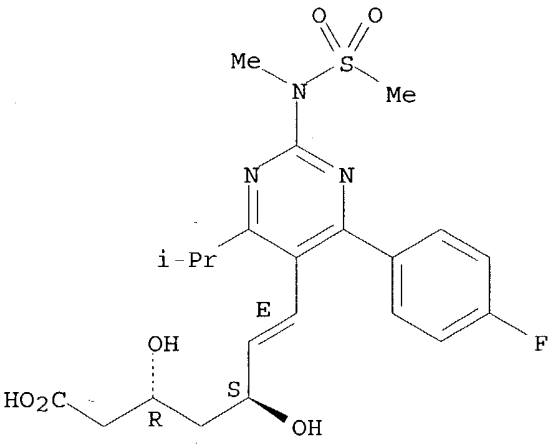
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 118:254949

L13 ANSWER 35 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 147098-20-2 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, calcium salt (2:1), [S-[R*,S*-(E)]]-
OTHER NAMES:
CN Crestor
CN Rosuvastatin calcium
CN Rosuvastatin hemicalcium
CN S 4522
CN ZD 4522, calcium salt
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . 1/2 Ca
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CHEMCATS, CIN, DIOGENES, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PHAR, PROMT, PROUSDDR, PS, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
CRN (287714-41-4)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



●1/2 Ca

72 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
74 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:374557

REFERENCE 2: 141:306673

REFERENCE 3: 141:288854

REFERENCE 4: 141:271570

REFERENCE 5: 141:156950

REFERENCE 6: 141:106490

REFERENCE 7: 141:54359

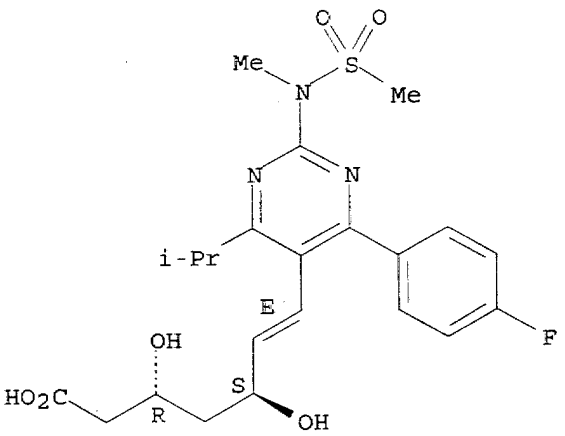
REFERENCE 8: 140:417696

REFERENCE 9: 140:302423

REFERENCE 10: 140:253443

L13 ANSWER 36 OF 36 REGISTRY COPYRIGHT 2004 ACS on STN
RN 147098-18-8 REGISTRY
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, monosodium salt, [S-[R*,S*-(E)]]-
OTHER NAMES:
CN Rosuvastatin sodium salt
FS STEREOSEARCH
MF C22 H28 F N3 O6 S . Na
SR CA
LC STN Files: BIOTECHNO, CA, CAPLUS, CHEMCATS, EMBASE, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: PREP (Preparation); PRP (Properties); RACT (Reactant or reagent)
CRN (287714-41-4)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



● Na

8 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:187485

REFERENCE 2: 140:120212

REFERENCE 3: 139:395947

REFERENCE 4: 136:64119

REFERENCE 5: 135:293982

REFERENCE 6: 135:183499

REFERENCE 7: 126:238350

REFERENCE 8: 118:254949

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